

Validation documentation
APIs & excipients, solid

HiperScan GmbH

July 14, 2020

Contents

Introduction	9
Context of this document	9
Criteria for the inclusion of substances	10
Validation concept	11
Model creation procedure and validation runs	11
Particularities of individual substance classes	14
Significance of testing with <i>Apo-Ident</i>	15
Conclusion	15
Explanation of terminology	16
Summary	21
Validation samples	21
Validation results	22
Validation reports	23
5-aminolevulinic acid hydrochloride	23
Acacia, dried dispersion	29
Acetylcysteine	35
Acetylsalicylic acid	41
Aciclovir	47
Albendazole	51
Alfatradiol	55
Allantoin	63
Allopurinol	69
alpha-tocopheryl acetate dry concentrate	73
Ambroxol hydrochloride	79
Amifampridine	85
Amitriptyline hydrochloride	91
Amphotericin B	97
Arginine	103
Arginine hydrochloride	109
Ascorbic acid	115
Ascorbyl palmitate	121
Atropine sulfate	127
Bacitracin	133
Beclometasone dipropionate	139
Benzocaine	145
Benzoic acid	153
Benzydamine hydrochloride	159
Betaine monohydrate	165
Betamethasone dipropionate, micronized	169
Betamethasone valerate	179
Betamethasone, micronized	197
Bifonazole	203
Biotin	209
Bismuth gallath, basic	215
Boric acid	223
Budesonide, micronized	229
Butylated hydroxytoluene	237
Caffeine	245
Calcium ascorbate	251
Calcium citrate tetrahydrate	257
Calcium gluconate	263
Calcium glycerophosphate	271
Calcium lactate pentahydrate	277

Calcium orotate dihydrate	283
Calcium pantothenate	289
Camphor, racemic	295
Cannabidiol	299
Capsaicin	305
Captopril	311
Carbomers 35000 / 50000	319
Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)	327
Cellulose, microcrystalline	333
Cetostearyl alcohol	339
Chloral hydrate	351
Chloramphenicol	359
Chlorhexidine diacetate	371
Chlorocresol	379
Chlortetracycline hydrochloride	385
Cholesterol	391
Choline chloride	397
Choline hydrogen tartrate	401
Ciclopirox olamine	407
Ciclosporin	413
Ciprofloxacin hydrochloride	421
Citric acid	425
Citric acid monohydrate	441
Citrulline	447
Clindamycin hydrochloride	453
Clioquinol	461
Clobetasol propionate	471
Clonidine hydrochloride	485
Clotrimazole	489
Colistin sulfate	507
Cyanocobalamin	513
Cyproterone acetate	519
Cystine	525
Dapsone	529
Dequalinium chloride	533
Dexamethasone	541
Dexamethasone acetate	553
Dextromethorphan hydrobromide monohydrate	559
Diclofenac sodium	563
Diltiazem hydrochloride	571
Dimethyl fumarate	585
Diphenhydramine hydrochloride	589
Dithranol	595
Doxycycline hyclate	603
Doxylamine hydrogen succinate	609
Enalapril maleate	615
Eosin Y	619
Ephedrine hydrochloride	625
Epinephrine hydrogen tartrate	631
Erythromycin	637
Escin, water-soluble	655
Estradiol benzoate	659
Estradiol hemihydrate	667
Estradiol valerate	675
Estriol	683
Ethacridine lactate monohydrate	691
Ethinylestradiol	697

Ethosuximide	703
Ethyl hydrogen fumarate calcium	707
Fampridine	713
Finasteride (form III)	719
Fluocinolonacetonid, micronized	725
Folic acid hydrate	731
Fructose	737
Furosemide	747
Fusidic acid	753
Galactose	759
Gelatine, white	765
Gentamicin sulfate	771
Glucose	783
Glucose monohydrate	791
Glutamic acid	803
Glutamine	807
Glycine	811
Glycopyrronium bromide	817
Gramicidin	821
Griseofulvin	827
Guaifenesin	833
Heparin sodium	839
Histamine dihydrochloride	845
Histidine	851
Hyaluronic acid sodium salt	855
Hydrochlorothiazide	859
Hydrocortisone	865
Hydrocortisone acetate	879
Hydroquinone	893
Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s)	899
Hyoscine butylbromide	913
Hyoscine hydrobromide	917
Ibuprofen	923
Indometacin	927
Inositol	933
Iodoform	937
Ipratropium bromide	943
Isoleucine	947
Isosorbide dinitrate 40%	953
Isoxuprine hydrochloride	961
Ketamine hydrochloride	965
Ketoconazole	971
Lactose monohydrate	977
Levocarnitine	991
Levothyroxin sodium	995
L-glutathione	999
Lidocaine	1003
Lidocaine hydrochloride monohydrate	1013
Lithium orotate monohydrate	1027
L-leucine	1031
L-malic acid	1035
L-phenylalanine	1039
L-proline	1045
L-threonine	1049
L-tryptophan	1053
Lysine hydrochloride	1059
Macrogols 1500	1065

Macrogols 4000	.1071
Magnesium citrate	.1083
Magnesium hydrogen aspartate tetrahydrate	.1089
Magnesium hydrogen citrate	.1093
Magnesium orotate dihydrate	.1101
Magnesium stearate	.1107
Manganese orotate dihydrate	.1113
Mannitol	.1117
Melatonin	.1131
Menthol	.1141
Mepivacaine hydrochloride	.1153
Mesalazine	.1157
Metamizol sodium monohydrate	.1163
Methacholine chloride	.1167
Methionine	.1173
Methoxsalen	.1179
Methyl-4-hydroxybenzoate	.1185
Methylcellulose	.1193
Methylcobalamin	.1201
Methylprednisolone	.1207
Metoclopramide hydrochloride	.1211
Metoprolol tartrate	.1215
Metronidazole	.1221
Miconazole nitrate	.1239
Minoxidil	.1251
Mometasone furoate, micronized	.1265
Monostereates	.1277
Mupirocin calcium	.1285
Naloxone hydrochloride dihydrate	.1289
Naphazoline hydrochloride	.1295
Naphazoline nitrate	.1301
Naproxen	.1305
Neomycin sulfate	.1309
Neostigmine bromide	.1317
Nicotinamide	.1323
Nicotinic acid	.1329
Non-ionic emulsifying alcohol	.1333
Norethisterone acetate	.1339
Nystatin	.1345
Octenidine dihydrochloride	.1353
Ofloxacin	.1361
Omeprazole	.1367
Ornithine aspartate	.1373
Ornithine hydrochloride	.1377
Oxalic acid	.1381
Oxetacaine	.1387
Oxybuprocaine hydrochloride	.1391
Oxybutynin hydrochloride	.1397
Oxytetracycline hydrochloride	.1403
Pancreas powder	.1411
Papaverine hydrochloride	.1415
Paracetamol	.1421
Patent blue V	.1427
Phenazone	.1433
Pheniramine maleate	.1439
Phenylbutazon	.1445
Phenylephrine hydrochloride	.1449

Phenytoin	1455
Pilocarpine hydrochloride	1459
Poloxamers 407	1465
Polymyxin B sulfate	1471
Potassium citrate	1477
Potassium hydrogen tartrate	1485
Potassium sodium tartrate tetrahydrate	1491
Potassium sorbate	1495
Potassium tartrate hemihydrate	1505
Povidone 25, soluble	1511
Povidone iodine	1517
Prasterone	1523
Prednicarbate, micronized	1529
Prednisolon dihydrogen phosphate dinatrium	1541
Prednisolone acetate	1547
Prednisolone hydrogen succinate	1559
Prednisolone, micronized	1563
Prednisone	1575
Pregnenolone	1581
Prilocaine hydrochloride	1587
Procaine hydrochloride	1593
Progesterone, micronized	1599
Promethazine hydrochloride	1613
Propranolol hydrochloride	1617
Propyl-4-hydroxybenzoate	1625
Propyphenazone	1631
Pyridoxal-5-phosphate	1637
Pyridoxine hydrochloride	1643
Quinidine sulfate dihydrate	1649
Quinine dihydrochloride	1653
Quinine hydrochloride	1657
Quinine sulfate	1663
Quinoline yellow	1667
Quinolinol sulfate potassium sulfate	1673
Resocrinol	1679
Ribavirin	1685
Riboflavin	1689
Riboflavin phosphate sodium	1695
Ropivacaine hydrochloride monohydrate	1699
Saccharin sodium	1703
Salicylic acid	1709
Selenium yeast	1723
Serine	1727
Sildenafil citrate	1731
Sodium acetate trihydrate	1737
Sodium ascorbate	1743
Sodium benzoate	1749
Sodium citrate	1757
Sodium cromoglicate	1769
Sodium cyclamate	1775
Sodium edetate	1781
Sodium methyl-4-hydroxybenzoate	1789
Sodium salicylate, powdered	1795
Sodium tetraborate	1799
Sorbic acid	1805
Sorbitol	1811
Soy lecithin (instant form)	1819

Spironolactone	.1825
Starch	.1833
Stearic acid 50	.1841
Sucrose	.1847
Sulfacetamide	.1859
Sulfadiazine	.1865
Sulfogaiacol hydrate	.1871
Tannin	.1875
Tartaric acid	.1883
Taurine	.1891
Testosterone	.1897
Testosterone propionate	.1905
Tetracaine base	.1915
Tetracaine hydrochloride	.1923
Tetracycline hydrochloride	.1933
Thalidomide	.1941
Theophylline	.1945
Theophylline-ethylenediamine hydrate	.1949
Thiamine chloride hydrochloride	.1953
Thymol	.1959
Tobramycin sulfate	.1965
Tosylchloramide sodium	.1971
Tranexamic acid	.1977
Tretinoin	.1983
Triamcinolone acetonide	.1993
Triamcinolone, micronized	.2013
Triclosan	.2019
Trometamol	.2039
Tropicamide	.2049
Tyrosine	.2053
Tyrothricin	.2057
Ubidecarenone	.2063
Urea	.2069
Uridine	.2085
Valine	.2091
Vancomycin hydrochloride	.2095
Vanillin	.2101
Waxes / Fats	.2107
Wool alcohols	.2129
Xylitol	.2135
Xylometazoline hydrochloride	.2141
Xylose	.2147
Zinc acetate dihydrate	.2153
Zinc gluconate	.2159
Appendix	2165
Additional calibration samples (<i>Type A</i>)	.2165
Additional validation samples (<i>Type B</i>)	.2171
Additional validation samples (<i>Type C</i>)	.2191
Requirements of validation	.2321
Conformity of <i>Apo-Ident</i> with the <i>European pharmacopeia</i>	.2322
Addition to the second-stage models	.2323
References	2325
Index	2327

Introduction

The unequivocal proof of the identity of pharmaceutical raw materials based on a monograph or traditional alternative methods is work-intensive, time-intensive and economically often no longer makes sense. Near-infrared spectroscopy (NIR) provides a new means here. It enables relatively easy, fast and nonetheless safe identity testing via the preparation and evaluation of spectra.

The analysis system *Apo-Ident* was developed specially for pharmacy use. Pharmacists have the duty to check the identity of all raw materials for extemporaneous products in their pharmacies. This normally takes place based on the monographs for the respective substances in the European Pharmacopoeia. But also NIR spectroscopy is described in the European Pharmacopoeia as an identification method which, as opposed to the methods incorporated in the respective monographs, is approved for testing [1] (quotation translated)

with the prerequisite that the same results (“namely the determination of the identity” [2]), (quotation translated) are achieved as with the described methods and instruments.

The *Apo-Ident* analysis system serves to identify raw materials for prescriptions in the defined manner according to *ApBetrO* [Pharmacies Rules and Regulations] §§ 6 and 11 at pharmacies (NIR spectroscopy as an alternative testing method). *Apo-Ident* consists of three components:

- An *NIR spectrometer*, which records the spectra of non-preprocessed raw materials in a measuring glass in diffuse reflection or transfection.
- The *QuickStep* spectroscopy software controls the instrument and records the spectra and user inputs via a pharmacy-specific software plug-in. It also generates the test protocol for documentation of the testing and storage of the printout to be signed in the pharmacy.
- The software module *IdentModule* incorporates *reference databases*. The spectra from the *QuickStep* software are presented to it for evaluation.

NIR spectroscopy is a very powerful analytical method. It is also able to establish the identity of several chemical compounds and mixes in as far as an appropriate database (technically correct: a [chemometric model](#)) was created. Identity testing with *Apo-Ident* is a very safe, very fast and easy to operate analytical method for testing a large number of raw materials.

Context of this document

The suitability of the instrument, method and database is proven as follows:

- *NIR spectroscopy as a method for identity testing*: The *Ph. Eur.* [3] describes NIR spectroscopy in *Section 2.2.40* as an analytical method which is also suitable for the identification of raw materials. Therefore, validation of the method as such is not necessary.
- *Performance of the instrument*: The *Ph. Eur.* [3] furthermore describes the apparatus and the testing of its performance in *Section 2.2.40*. The document *Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident* [4] compares the implementation by *Apo-Ident* with this monograph in order to prove that *Apo-Ident* meets the specifications of the Pharmacopoeia. Each individual instrument delivered to a pharmacy is qualified in accordance with the tests described in “*Control of Instrument Performance*”. In this test, the unit consisting of analysis instrument hardware and the *QuickStep* spectroscopy software is assessed. The result is documented in a test protocol which is kept at the pharmacy.
- *Validation of the database* is documented separately for each substance class. The report at hand documents the substance class *APIs & excipients, solid*.

The *Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD)* [Working Group of German Pharmacy Inspectors] has clarified the following in its resolution dated October 16, 2013 ([5], quotation translated):

NIR is a testing method incorporated in the Pharmacopoeia. The testing quality depends on the quality of the database stored. The APD views the use of NIR instruments in case of ensured validation of the databases used in conjunction with it as one of several options for identity testing.

The APD defined more precisely ([6], quotation translated) on October 1, 2014:

The use of near-infrared is a recognised testing method according to Ph. Eur. 8. For the use of NIR instruments in pharmacies for testing the identity of raw materials, sufficient and verifiable validation of the instrument used is required. The quality of the database stored by the instrument manufacturer is decisive for quality. Batch-specific differences with the same original substances must be taken into account if present.

So NIR is basically suitable. The validity of the reference database is proven with the existing validation documentation.

Criteria for the inclusion of substances

This validation documentation describes the results of the validation of the reference database for the substance class *APIs & excipients, solid*. Validation documentation is created for each published version of the reference database for all substance classes incorporated.

The reference database is incorporated in the software module *IdentModule*. During identification testing with *Apo-Ident*, spectra which are used for evaluation purposes are presented to it by the *QuickStep* software. In the same manner, the *IdentModule* is presented all validation spectra successively during the validation runs for evaluation purposes. The *IdentModule* responds respectively (without taking the initial assumption into account) with the identified substance or rejects it as unknown. The correctness of this response is checked for each possible initial assumption and counted.

The results are summarised for each substance and reproduced in this document. The core statement of this validation report is that the following criteria must be fulfilled for each database entry, so that *Apo-Ident* offers verification of identity by means of NIR for the relevant substance/substance group:

- The database is exclusively generated from spectra which have been recorded by *HiperScan GmbH* on traceable samples in pharmaceutical quality.
 - The samples are procured via typical pharmacy sources (*DAC III.2.: Bezugsquellennachweis für Rezepturbestandteile [reference source for prescription components]* [7]).
 - A valid manufacturer's certificate exists (content, purity and identity of the batch).
 - The identity was confirmed by a certified test laboratory or *HiperScan GmbH*.
- Each version of the reference database (every update) is validated in-full.
 - Calibration spectra (*Type A*), other spectra recorded under the control of *HiperScan GmbH* (*Type B*), and spectra from the field (*Type C*) are presented to the *IdentModule* for evaluation in three separately evaluated validation runs.
 - Here, no single *false positive* result may arise.
 - Here, the various substance classes are also tested for reciprocal rejection, where this is objectively justified (see *Summary* section).
- In the validation with spectra recorded under the control of *HiperScan GmbH*, spectra of at least one independent sample must be considered, i.e. spectra from a batch whose spectra have not been used for the generation of the database. In addition, the set of *Type A* and *Type B* spectra must originate from at least three different batches.
- Spectra of additional substances may be used for the generation of the database even though they will not be offered for identification by this database. The purpose is the reliable distinction from these substances.

- Any positive result of *Apo-Ident* confirms the identity of the substance/substance group and distinguishes it from all other substances of the database. In the case of substance groups, the result is ambiguous: Distinction from all substances not belonging to the group is proven. The substance is identified as a member of this group. However, within the substance group, it is not possible to reliably classify which substance has been tested.
- The criteria for clear identifiability are a [specificity](#) of 100 % ([true negative rate](#)) and a minimum distance in the distance matrix. See 2. d) under [Model creation procedure and validation runs](#).

Validation concept

[Chemometrics](#) is a statistical technique for the extraction of relevant chemical information from spectra. In mathematics, this method is described as *multivariate data analysis*. Chemometrics proceeds here as follows:

1. Collection of spectra for the *calibration sample*. The results (identities) of the calibration sample must be known. The calibration samples must be representative for the samples which are to be evaluated later. Therefore, they must take the various possible (physical) compositions into account. (Therefore, sourcing calibration samples for NIR from the specialist trade is superior to the use of CRS reference substances.)
2. The first mathematical step is *calibration*. Here, the [chemometric model](#) is calculated from the *calibration sample spectra* ([reference spectra](#)) and limits as well as some parameters are stipulated. The chemometric model is used later to calculate the analysis result (*prediction*).
3. Collection of further spectra for the *validation sample* which should be independent of the *calibration sample*. The results (identities) of the *validation sample* must also be known. The textbook suggests a random sample with a normal scope of 25 % to 50 % of the *calibration sample* [8].
4. The second technical data step is *validation*. Here, the [chemometric model](#) created is evaluated based on the spectra of the *validation samples*. As validation parameters for the identification, the *Ph. Eur. Section 2.2.40* [3] specifies the [specificity](#) and [robustness](#).

The validation step according to the textbook has the target of estimating the performance capability of the model created based on a random sample. In order to achieve the best possible precision, attention is paid to the calibration sample. In the field of pharmaceuticals, the safety of the method has priority. In order to be able to [validate](#) the model within the regulatory scope, the validation step must include probative force. For this purpose, the validation sample must be *representative and complete* in order to enable the testing of all cases.

A *sufficient number of batches* must be secured for validation because validation finally proves whether the number of batches in calibration suffices.

Each substance is validated individually. The validation results are documented per substance in this document. Moreover, the documents show how many and which batches have been used for creating the model or model validation.

At least one certificate is taken in for each substance from an accredited test laboratory for the independent testing of identity of the sample. The identification number of the corresponding test certificate is listed in the report, enabling traceability of a substance tested according to the monographs in the Pharmacopoeia.

Model creation procedure and validation runs

The safety of the [chemometric models](#) is guaranteed by several measures during model creation, of which the validation step is the final one. Normally, the procedure is as follows. It is in particular valid for the active pharmaceutical ingredients (APIs) *solid API excipients, liquid/semi-solid API excipients (with a test certificate), narcotics - solid medicinal substances and drugs*. If, for individual substance classes, variations are required, they are depicted in the section [Particularities of individual substance classes](#).

1. Collecting the reference spectra (calibration sample)

- a) Procurement of the samples from the same sources from which pharmacies source their raw material for compounding (Caelo, Fagron, Euro-OTC, ..., see also *DAC III.2. Bezugsquellen-nachweis für Rezepturbestandteile* [Sources of supply for compounding] [7]).
- b) Testing the suitability according to *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, that is to say the availability of a valid manufacturer certificates via identity, purity and contents of the batch.
- c) Recording standard 40 spectra of the sample in different positions, as a standard on four instruments. Here, handling and presentation of the samples as later in the pharmacy.
- d) Visual checking for anomalies in the spectra. In case of indications of measurement errors, measurement must be repeated. If a signature is missing in the spectrum, the substance may be excluded from the start as not promising (the spectra are nonetheless entered in the database validation as independent *Type B* spectra).
- e) Testing identity. For each substance, a certificate of correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the respective following substance page of this validation documentation the *Mahalanobis distance* to this reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance. Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

HiperScan GmbH cooperates with some suppliers as follows: the raw materials supplier takes a sufficiently large sample in his incoming goods area so that part of it can be used for recording the NIR spectra. The remainder of the sample goes to analytics for market approval. The manufacturer's batch certificate emerges from these identity, contents and purity tests, which consequently also prove the correct identity of the NIR reference sample. Therefore, the NIR spectra are suitable for structuring the database (*Type A*) and can also optionally be used for validation (*Type B*). The samples which this applies to are marked in the validation report with a footnote.

- f) If the identity of the new sample is proven, it is declared as a reference sample and the spectra are approved for structuring the database.

2. Generating the chemometric models (calibration)

- a) Determination of the transformation matrix from the reference spectra using variance maximisation [8, 9]. (All reference spectra are always included, even if only a few spectra are added for an update.) All reference spectra receive the same data pre-treatment, which is also later applied to all measurement spectra in the field (in the pharmacies).
- b) Checking that the number of principal components used is still sufficient.
- c) Calculating the limits for each substance from the spread of the reference spectra. The calculation regulation is identical for each substance in a substance class.
- d) Überprüfen der Abstände zwischen den Grenzen der trennbaren Substanzen: Die Distanzmatrix enthält die *Mahalanobis-Abstände* von jeder Substanz zu jeder anderen. Die Werte hin und zurück sind jeweils unterschiedlich, weil die Streuung der Ausgangssubstanz eingeht. Ist eine Distanz kleiner als der Mindestabstand, so gelten die Substanzen als nicht sicher trennbar. Der Mindestabstand ist auf 9 festgelegt. Der Entwickler des Modells darf einen größeren Mindestabstand festlegen (ein Wert für das gesamte *chemometrische Modell*), um die Trennschärfe zu erhöhen.
- e) Überprüfung des Modells anhand der Referenzspektren. Es sind keine *falsch-positiven* Ergebnisse erlaubt.

f) Wird eines der Kriterien verletzt (d) *Unterschnittener Mindestabstand zwischen zwei Substanzen* oder (e) *Eine Substanz wird als eine andere identifiziert*, entscheidet der Entwickler der Datenbank, welche der folgenden Optionen er anwendet:

- Er nimmt beide Substanzen aus der Datenbank. (Die Spektren bleiben in der Validierung und dürfen auch in den Aufbau eingehen. Sie werden aber nicht zur Prüfung angeboten.)
- Er bildet eine Substanzgruppe mehrerer nicht sicher trennbarer Substanzen. Dann ist das Ergebnis mehrdeutig: Das chemometrische Modell stellt fest, dass es sich bei der Probe um eine der Substanzen aus der Gruppe handelt und dass es sich um keine andere Substanz handelt. Es kann aber nicht sagen, um welche der Substanzen es sich handelt. Um die eindeutige Identität festzustellen, muss der Anwender eine geeignete ergänzende Prüfung durchführen.
- Er erstellt ein weiteres *chemometrisches Modell* mit geringerem Umfang, in das mindestens alle Substanzen der nicht sicher trennbaren Substanzgruppe eingehen (Zweite-Stufe-Modell). Zweite-Stufe-Modelle werden nur aufgerufen, wenn die erste Stufe festgestellt hat, dass es sich nur um eine der Substanzen handeln kann, die in den Aufbau der Zweiten Stufe eingegangen ist. Die Zweite-Stufe-Modelle sind im Anhang *Zusatz zu den Modellen der zweiten Stufe* dokumentiert.

3. Set of validation spectra (validation samples)

The following is provided for validation:

- a) *Type A*: The reference spectra = calibration spectra from which the database was generated. These also include spectra from substances which the *chemometric model* should not identify, but were also recorded during generation in order to increase selectivity. (As a result, the model “learns” to differentiate from other substances which are actually unknown to it.)
- b) *Type B*: Spectra recorded under the control of *HiperScan GmbH* and not used for the generation of the database. These also include reference spectra of other substance classes, and spectra that are not used as reference spectra. Samples are considered to be independent, if they originate from a batch, of which no spectra have been used for the generation of the database. (Up to *IdentModule 2018-01*, samples were still considered independent if the sampling was done independently, i.e. if they originate from another sales container.)
- c) *Type C*: Spectra from the field, which have not been recorded under the control of *HiperScan GmbH* and have not been used for the generation of the database. The spectra include not only substances of the substance class to be tested, but also substances from other classes.

All manufacturers’ batches from which spectra are used for the validation are listed by substance in this document: for substances included in the substance class *APIs & excipients, solid* in the respective validation reports; otherwise in attachments *A*, *B* and *C*.

Furthermore remains valid: validation spectra may only be removed if a error in the spectrum can be proven. Here, the spectra are not deleted, but instead placed on a *blacklist* incorporating the reason, date and initials in the commentary.

The section *Particularities of individual substance classes* treats the other substance classes from which *Type B* and *Type C* spectra are cited for validation purposes.

4. Validation runs and approval

- a) Validation spectra are transferred holistically to the *IdentModule* for evaluation in the same way as the spectroscopy software *QuickStep* transfers measured spectra.
- b) Following the provision of each spectrum, the *IdentModule* responds as to whether it has recognised a substance and which substance was recognised.
- c) The correctness of this response is checked for each possible initial assumption (each measurable substance with the substance class) and counted according to *true negative*, *false negative*, *true positive* and *false positive*. These figures are provided for each substance and additionally in the section *Summary*, separated according to types *A*, *B* and *C*.

- d) No *false positive* results whatsoever are permissible.
- e) If the criterion is also met for all substance classes, the *IdentModule* is approved.

Particularities of individual substance classes

Basically, *HiperScan GmbH* procures and tests the manufacturer's certificate for the batch, commissions external testing of the identity of the sample or carries it out independently and stores the certificates. As described, this process is established for the Pharmacopoeia substances, that is to say for substance classes **APIs & excipients, solid**, **APIs & excipients, liquid/semi-solid (with analysis certificate)**, **Narcotic substances, liquid/semi-solid** and **Drugs**. Therefore, *HiperScan GmbH* is able to furnish proof of the identity of the reference samples. In case of manufacturer-specific substance classes and others, individual steps are organised differently in-part:

The substance class **APIs & excipients, liquid/semi-solid (other)** (often described as cosmetics) incorporates substances for which no specification of the requirements of the pharmaceutical quality is determined, neither in a Pharmacopoeia monograph, a DAC/NRF monograph nor via a manufacturer's specification. Consequently, neither the identity nor contents can be tested independently. No certificates whatsoever exist for the reference samples. So here, merely the matching of the sample with former samples of this product is established and confusion with the other substances is ruled-out. (If the manufacturer of such a substance prepares a specification, determines testing methods and provides manufacturer's certificates in accordance with *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, *HiperScan GmbH* can assign the substance to the substance class *APIs & excipients, liquid/semi-solid (with analysis certificate)* again in the future).

Substance class **HCK – nutritional supplements (Hepart)** contains the HCK micro-nutrients from the Swiss company *Hepart AG*. *HiperScan GmbH* receives the reference samples directly from the manufacturer. For each reference sample, *HiperScan GmbH* also receives manufacturer's certificates and keeps these. New checking of the identity of the reference sample is not carried out by *HiperScan GmbH*. The identity of the reference samples is therefore documented by *Hepart AG*. The spectra of all batches provided by *Hepart AG* are recorded by *HiperScan GmbH* and entered in the database.

All the manufacturer's batches are used for the generation and validation of the substance class **HCK**. The expected variation is also represented in the generation and validation if there are less than three batches.

Also, for the substance class **PhytoComm** (TCM-Granulated herbal extracts of the manufacturer *PhytoComm*) spectra for all useable batches are recorded by *HiperScan GmbH* and entered in the database. The supplier organises the respective tests themselves and keeps the test certificates.

A new evaluation option was created for the class *PhytoComm* with the update 2016-01. As the risks are considerably fewer than those from chemical agents, the pharmacist can specify a reasonable criterion for the *specificity* in accordance with internal risk estimation. The database for this is created without taking safety distances into account and no criterion is determined in advance for the *specificity*. Instead, the *specificity* for testing the identity with this concrete substance is calculated in the validation for each substance and provided with the measurement result. The pharmacist then judges himself whether this safety is reasonable with regard to the risk of the substance.

Additionally, a statistical forecast is provided for the *specificity* which is determined according to the *Rule of Three* [10, 11]. For this forecast, it is assumed that there would have been three wrong results more and is provided with a lower limit for *specificity*. This value has a special meaning if a *specificity* of 100 % is achieved for a substance during validation. In this case, the lower limit allows conclusions regarding the scale of existing safety for which with an endless number of validation spectra a value of less than 100 % is to be assumed.

If, for example 14 000 spectra not belonging to the substance are presented and no *false positive* classification is made, a hypothetical number of three *false positive* results is assumed (*Rule of Three* [10, 11]) and the *specificity* is defined with 100.0000 % (> 99.9786 %). Here, it applies that the higher the number of validation spectra which form the statistical basis, the better the *specificity* calculated via the lower *specificity* limit will be approximated.

The positive result of the identity test using *Apo-Ident* establishes that the sample spectrum is in accordance with a batch of the specified granulate from the supplier *PhytoComm*, whereby all useable batches from the supplier are known.

The *PhytoComm* class can only confirm the identity of batches that have been used for the generation of the database. As a consequence there cannot be any validation spectra of other batches. Therefore, the criterion reads that two samples (from different sales containers) from each batch must exist, one for the structure of the database (*Type A*) and one for the validation (*Type B*).

Significance of testing with *Apo-Ident*

The analysis result is determined using sophisticated statistical methods according to state-of-the-art science and technology. Chemical and pharmaceutical knowledge is applied for the selection of the samples from which the calibration spectra and validation spectra are recorded. Otherwise it does not influence the further steps of model creation.

Verbally, the statement of the analysis result can be expressed as follows. Here “*the spectra match*” means that the criteria *Mahalanobis distance*, *outlier analysis* and *correlation* are met as shown in *Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident* [4]. “The spectra do not match”, on the other hand, means that at least the criterion *Mahalanobis distance* is not met.

The positive analysis result “*was identified as ...*” is very meaningful because both the quantity of substances to be taken into account and the number of underlying samples is very comprehensive.

1. The spectrum of the sample measured matches spectra of the defined substance.
2. The spectrum of the sample measured does not match any spectrum of any other substance in this substance class. Therefore, all other substances can be clearly ruled-out.
3. As the spectra from other substance classes were used for validation, it is proven that no spectrum of one of these other substances matches the defined substance. (All substance classes with which a spectrum comparison is possible and makes sense are used for validation. This is documented for each substance class in the section *Summary*.)
4. If the defined substance belongs to a *substance group* which in itself is not clearly separable with *Apo-Ident*, matching with the spectra of one or several substances in this group is confirmed. Which of these substances it actually is cannot be determined clearly. All other substances are excluded analogous to 2 and 3.

On the other hand, a negative analysis result “*was not identified as ...*” means:

1. The substance offered could not be recognised based on the spectrum of this sample.
2. The identity of this sample is not confirmed.
3. Testing must be repeated in accordance with the specifications of the Pharmacopoeia.

Conclusion

NIR spectroscopy is a testing method incorporated in the Pharmacopoeia. In case of successful database validation, it is a possible method for identity testing [5]. *Apo-Ident* meets the criteria of the *European Pharmacopoeia* as a near-infrared spectrometer and proves the validity of the reference database with the existing validation documentation. This means that *Apo-Ident* can be used as an alternative testing method for testing raw materials at pharmacies.

Explanation of terminology

The following section serves to explain or define specialist terminology which is required in order to understand this document. If necessary, definitions for the analysis system *Apo-Ident* are defined more precisely.

The term database is used in this document exactly as in the *Ph. Eur. Section 2.2.40* [3] synonymous with [chemometric model](#). In order to differentiate the databases which are relatively independent of each other, *HiperScan GmbH* frequently also uses the term [substance class](#) (primarily in the plural). On the other hand, the spectra used to structure the database are termed spectrum collection and not database.

Substance classes are units of the organisational structure of the *IdentModule*. The substance classes are substance [databases](#) which are also broadly independently subscribable. On the one hand, the liquid and semi-solid substances are separated from the solid powders because they are measured against different references and therefore the spectra cannot be compared. On the other hand, for example the Pharmacopoeia substances are kept separated from the manufacturer-specific database *PhytoComm* for TCM (traditional Chinese medicine) raw materials.

The individual substance classes need only be limited against each other in-part. Often, no risk of confusion exists because they can only be procured from different sources. On the other hand, in several cases we handle substances which need not be distinguished. For example, em Huang Qi granulate from the company *PhytoComm* neither needs to be delimited from *Huang Qi* granulate from the company *HerbaSinica* nor is matching required. Respectively one single [chemometric model](#) is behind a substance class. (Even if several reciprocally secured chemometric models would be permissible.) The terms *substance class*, *chemometric model* and *databases* are mostly used here as synonyms.

A substance group respectively summarises all the substances within a [substance class](#) which cannot safely be distinguished from one another based on their NIR spectra. However, all the other substances in the database can be excluded.

The formation of subgroups is mentioned in the *Ph. Eur. Section 2.2.40* [3]. In this manner, technical restrictions in case of extensive databases can be avoided and it is possible to prepare individual subgroups with different spectrum pre-treatment. Validation of the subgroups against each other is required. *HiperScan GmbH* has solved these technical restrictions and doesn't use any subgroups within a substance class any longer.

Principal component analysis (PCA) [8, 9] is a multivariate statistics process or multivariate data analysis. It serves to structure, simplify and illustrate comprehensive data records by describing a large number of statistical variables by describing a lower number of linear combinations (the *principal components*) which are as significant as possible. In the *Apo-Ident IdentModule*, *PCA* is used to evaluate the recorded spectrum data (corresponding with *Ph. Eur. 2.2.40* [3]).

The term validation is defined in both relevant contexts here with different (even if related) meanings.

Within the sense of the expert discipline of *chemometrics*, validation is a process step when creating a [chemometric model](#): after a transformation matrix, limits and various parameters have been calculated or determined from a set of reference spectra during the course of the calibration step [8, 9], the validation step determines the performance capability of the model (selectivity, precision, ...) based on the validation spectra. Normally, random sampling is planned here. In order for the validation to gain strength of proof, the validation spectrum set must be selected with an appropriately wide scope (*representative* and *complete*). The terms *validation run* and *validation step* always actually mean the process step in this sense.

In the regulatory sense (of pharmaceutical production), validation is the documented proof that a process or system meets the previously specified requirements reproducibly when applied practi-

cally. In this sense, the *Apo-Ident* databases only become validated databases with the validation documentation, which this document is part of.

The *European Pharmacopeia* uses the term validation in *Section 2.2.40* within the sense of the specialist discipline of *chemometrics* [3].

The robustness of a process is the property of only being influenced by environmental fluctuations (e.g. temperature or humidity) a little. A method is robust if the environmental conditions do not or hardly falsify the final result.

The specificity of a classification (of a [chemometric model](#)) is the [true negative rate](#).

The recognition rate (also sensitivity) is the [true positive rate](#). It defines in how many percent of cases a correctly set up substance is actually confirmed.

The true negative rate describes the share of spectra correctly classified as non-identity during validation. This is equivalent to correct classification. It means that a substance *A* within identity checking as substance *B* is judged as “*not identified*”. The *true negative rate* is equivalent to the conditional frequency

$$h(\text{rejected}|\text{genuinely no identity}) = \frac{r_n}{r_n + f_p}$$

with r_n as the total number of *true negative* classifications and f_p as the total number of *false positive* classifications. For successful validation of an *IdentModule*, all spectra presented belonging to this category must be classified as *not in accordance*.

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of this number. The weight of each spectrum of a substance/substance group *i* therefore results as

$$w_i = \frac{1}{n_i}$$

with n_i number of spectra in this substance/substance group. This weighting ensures that the overall result cannot be enhanced by adding especially large numbers of spectra from easily separable substances.

The true positive rate describes the share of spectra correctly classified as identity during validation. This is equivalent to correct classification. It means that a substance *A* within identity checking as substance *A* is judged as “*identified*”. The *true positive rate* is equivalent to the conditional frequency

$$h(\text{identified}|\text{genuine identity}) = \frac{r_p}{r_p + f_n}$$

with r_p as the total number of *true positive* classifications and f_n as the total number of *false negative* classifications. The *true positive rate* is a measure for the recognition rate of the validated *Apo-Ident IdentModule*.

In order to ensure that each substance is received with the same weight, the spectra are weighted as described for the [true negative rate](#).

The true negative result describes a spectrum correctly classified as non-identity during validation. It is equivalent to correct classification. It means that a substance *A* within identity checking as substance *B* is judged as “*not identified*”.

The false positive result describes a spectrum falsely classified as non-identity during validation. This is the most critical type of possible false classification. It means that a substance *A* within identity checking as substance *B* is judged as “*identified*”. For successful validation of an *IdentModule*, a number of false positive events of zero are demanded for all spectra entering the validation. The exception to this restriction is the class of TCM granulates from the company *PhytoComm* as described under [Particularities of individual substance classes](#).

The true positive result describes a spectrum correctly classified as identity during validation. It is equivalent to correct classification. It means that a substance *A* within identity checking as substance *A* is judged as “*identified*”.

The false negative result describes a spectrum falsely classified as non-identity during validation. It is equivalent to false classification. It means that a substance *A* within identity checking as substance *A* is judged as “*not identified*”.

The ‘Rule of Three’ says that with a probability of 95 % the next random sample of the same size no more than three false results are to be expected if no false result existed in the existing random sample [10, 11].

The *specificity* and *recognition rate* are determined both globally and from the validation runs for all substances. The information is supplemented with the hypothetical value if there had been three false results more. The percent information is provided in parentheses with the “greater than” symbol ‘>’, e.g. *specificity* 100.000 % (>99.983 %) if 17 567 false spectra have been presented without one single *false positive* result. The larger the statistical basis, the lower the influence of the hypothetical false results.

The Mahalanobis distance is a distance measure between two points in *n*-dimensional vector space. Here, the respective direction component of the distance to *standard deviation* [12] of an *n*-dimensional distribution is standardised. In case of the *principal component analysis* [8, 9] this standardisation relates to the distribution of the respective calibration data set for a classification (substance/substance group) in the *principal component space* [8]. The *Mahalanobis distance* of a point (mapping of a spectrum) $\vec{y}$ in the *n*-dimensional principal component space to the expected value of an *n*-dimensional distribution $\mathbf{X}$ then results as

$$d(\mathbf{X}, \vec{y}) = \sqrt{(\bar{\mathbf{X}} - \vec{y})^T \mathbf{S}^{-1} (\bar{\mathbf{X}} - \vec{y})} \quad \text{with} \quad \mathbf{X} \in \mathbb{R}^{m \times n}, \vec{y} \in \mathbb{R}^m$$

[13]. Here, *m* is equivalent to the number of principal components used (dimension of the principal component space) and *n* the number of measurements existing in the calibration data set (spectra). $\bar{\mathbf{X}}$ is the expected value of the resulting distribution for the calibration data set (the average value of *n* measurements received). $\mathbf{S}^{-1}$ is the inverse covariance matrix [12] for distribution $\mathbf{X}$.

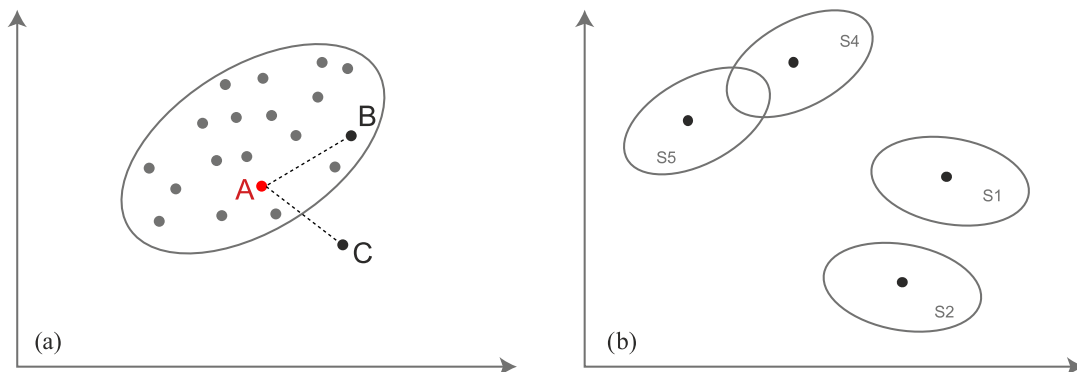


Figure 1: (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

The *Mahalanobis distance* offers advantages compared to the *Euclidean distance*: For the calculation of the distance it takes the statistical properties of a data point distribution (measurement series), i.e. average value, variance and covariance of the data points [14] into account. The *Mahalanobis distance* is applied while creating the reference database for evaluating the spectra from different samples of a substance.

A chemometric model is a classifier based on statistical methods [8, 9]. Through the respective algorithm used (e.g. *Principal Component Analysis*, *Cluster Analysis*), a maximum of chemical information is extracted from measurement data. Here, systematical or physical disturbances are eliminated using appropriate data pre-processing [15, 16].

At several places in this document, in order to simplify understanding, the term **database** is used instead of *chemometric model* – in the same manner as in the *Ph. Eur. Section 2.2.40* [3].

A sample (with its own sample ID) refers to substance in a sales container. Repeated sampling from the same sales container is listed under the same sample ID. (The suffix “SI” is not part of the sample ID.) Several samples may originate from the same batch. Samples are called “independent”, if they originate from a batch, of which no spectra have been used for the generation of the database. (Up to *IdentModule 2018-01*, samples from different sales packages were considered to be independent.) The information above the list of validation spectra now includes also the number of batches that deliver independent samples for the validation (for both *Type B* and *Type C*).

In case a supplier takes a sample for testing from its incoming goods and splits it to multiple laboratory containers, the substance in all laboratory containers will still be ascribed to the same sample. *HiperScan GmbH* only uses one of the subsamples.

Reference samples are used to structure the database. The *reference spectra* originate from these samples. In chemometric technical jargon you would normally say: For *calibration*, a **chemometric model** is generated from the *calibration spectra* recorded from the *calibration samples*, whose quality is subsequently assessed in **validation**.

Reference samples are procured via typical pharmacy sources. Their identity is tested. The *reference spectra* are recorded by *HiperScan GmbH*. The documentation also includes the manufacturer’s name and batch number.

Reference samples are clearly identified by a sample ID. Samples without sample ID may not be used as *reference samples*.

Summary

A total of 341 078 spectra from 35 450 different batches for a total of 876 substances were used to validate the substance class *APIs & excipients, solid*.

Validation samples

The validation samples can be categorised as follows:

Typ A Calibration spectra. These are the spectra used to generate the chemometric model. They were recorded by *HiperScan GmbH*. Detailed information regarding the batches or samples can be found in the following validation reports under *calibration samples* and under *Type A*. Further information is listed in [Appendix A](#).

Substance class	Substances	Batches	Spectra
APIs & excipients, solid	348	1848	101 728
Specific classifier 26188	11	23	1140
Narcotic substances, solid	15	75	6951
Drugs	17	20	870

From category *A* a total of 110 689 spectra from 1966 batches for a total of 391 substances were taken into account for validation.

Typ B Spectra from independent samples which are not included in database generation. These spectra were recorded by *HiperScan GmbH*. Detailed information regarding the batches or samples can be found in the following validation reports in the section *Type B* or in [Appendix B](#).

Substance class	Substances	Batches	Spectra
APIs & excipients, solid	508	1857	91 671
Drugs	263	489	22 533
Narcotic substances, solid	17	58	4089
Specific classifier 26188	12	19	849

From category *B* a total of 119 142 spectra from 2423 batches for a total of 800 substances were taken into account for validation.

Typ C Spectra from independent samples which are not included in database generation. *Apo-Ident* customers carried out the measurements. Detailed information regarding the batches or samples can be found in the following validation reports in the section *Type C* or in [Appendix C](#).

Substance class	Substances	Batches	Spectra
APIs & excipients, solid	405	26 042	95 967
Drugs	285	5895	14 068
Narcotic substances, solid	15	518	1207
Specific classifier 26188	2	5	5

From category *C* a total of 111 247 spectra from 32 460 batches for a total of 707 substances were taken into account for validation.

Validation results

The validation runs checked whether all substances/substance groups in the substance class *APIs & excipients, solid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, the matching of all relevant spectra of various substances with the substances/substance groups in the substance class *APIs & excipients, solid* was checked and the correctness of the results was evaluated. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	101 169	99	34 433 700
Type B	0	75 842	1510	37 094 356
Type C	0	90 876	2488	34 615 110

All substances/substance groups in the substance class *APIs & excipients, solid* can be clearly distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Typ A	100.000 00 % (> 99.999 97 %)	99.927 76 % (> 99.923 84 %)
Typ B	100.000 00 % (> 99.999 97 %)	98.164 48 % (> 98.156 75 %)
Typ C	100.000 00 % (> 99.999 65 %)	95.797 50 % (> 95.723 26 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **5-aminolevulinic acid hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20371-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

5-aminolevulinic acid hydrochloride; Acidum aminolaevulinicum hydrochloricum

Special notes

When selecting the *5-aminolevulinic acid hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
5-aminolevulinic acid hydrochloride	4	1	43

Second-stage model

For differentiation of the substance/substance group *5-aminolevulinic acid hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *5-aminolevulinic acid hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	5-aminolevulinic...	16357904	23208	40	1707616
Caelo	5-aminolevulinic...	16357904	23747	40	20170324
Caelo	5-aminolevulinic...	190219	24733	40	20190312*
Fagron	5-aminolevulinic...	13K27-N02	21339	40	20131125
Fagron	5-aminolevulinic...	17A12-B07-332960	23403	40	20170131
Fagron	5-aminolevulinic...	17A12-B07-332960	23404	40	20170131

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *5-aminolevulinic acid hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *5-aminolevulinic acid hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	5-aminolevulinic acid hydroc...	18C16-B05-347714	24099	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 60 spectra from 22 *Apo-Ident* customers from 44 batches from the substance/substance group *5-aminolevulinic acid hydrochloride*.
- Among them are spectra of independent samples from 43 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	5-aminolevulinic acid hydroc...	12093208	1
Caelo	5-aminolevulinic acid hydroc...	13017402	1
Caelo	5-aminolevulinic acid hydroc...	14145003	2
Caelo	5-aminolevulinic acid hydroc...	14145011	1
Caelo	5-aminolevulinic acid hydroc...	11355616	1
Caelo	5-aminolevulinic acid hydroc...	14145007	2
Caelo	5-aminolevulinic acid hydroc...	13K27-N02	1
Caelo	5-aminolevulinic acid hydroc...	13017403	1
Caelo	5-aminolevulinic acid hydroc...	15254803	1
Caeolo	5-aminolevulinic acid hydroc...	15254803	1
Fagron	5-aminolevulinic acid hydroc...	12c23-n05	1
Fagron	5-aminolevulinic acid hydroc...	12H20-N01	1
Fagron	5-aminolevulinic acid hydroc...	14K13-B01	1
Fagron	5-aminolevulinic acid hydroc...	12K26-N05	1
Fagron	5-aminolevulinic acid hydroc...	11I30-N01	1
Fagron	5-aminolevulinic acid hydroc...	7447	1
Fagron	5-aminolevulinic acid hydroc...	13J29-N03	2
Fagron	5-aminolevulinic acid hydroc...	15C06-B02-305245	1
Fagron	5-aminolevulinic acid hydroc...	15J23-B06	1
Fagron	5-aminolevulinic acid hydroc...	16A11-B02-317459	3
Fagron	5-aminolevulinic acid hydroc...	16A11-B02-318406	1
Fagron	5-aminolevulinic acid hydroc...	16A11-B02-316734	1
Fagron	5-aminolevulinic acid hydroc...	16I12-B06	1
Fagron	5-aminolevulinic acid hydroc...	15J23-B06-314284	1
Fagron	5-aminolevulinic acid hydroc...	16A11-B02	1
Fagron	5-aminolevulinic acid hydroc...	16G27-B10	1
Fagron	5-aminolevulinic acid hydroc...	17A12-B07-331745	1
Fagron	5-aminolevulinic acid hydroc...	17A12-B07-331744	1
Fagron	5-aminolevulinic acid hydroc...	17F01-B06_337165	1
Fagron	5-aminolevulinic acid hydroc...	17F01-B06-337164	2
Fagron	5-aminolevulinic acid hydroc...	17F01-B05-338204	1
Fagron	5-aminolevulinic acid hydroc...	16K17-B09-328197	1

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Supplier	Substance	Batch	Spectra
Fagron	5-aminolevulinic acid hydroc...	1701-b05-342090	1
Fagron	5-aminolevulinic acid hydroc...	17122-B02-343410	1
Fagron	5-aminolevulinic acid hydroc...	17L18-B05-344673	1
Fagron	5-aminolevulinic acid hydroc...	18C16-B05	2
Fagron	5-aminolevulinic acid hydroc...	18G13-B06	2
Fagron	5-aminolevulinic acid hydroc...	13C19-N05	3
Fagron	5-aminolevulinic acid hydroc...	13H13-N07	2
Fagron	5-aminolevulinic acid hydroc...	16I12-B06-326185	1
Fagron	5-aminolevulinic acid hydroc...	17/22-B02-342555	1
Fagron	5-aminolevulinic acid hydroc...	18C16-B05-347714	1
Fagron	5-aminolevulinic acid hydroc...	14K04-B01-297971	2
Caelo	5-aminolevulinic acid hydroc...	12093205	2
	5-aminolevulinic acid hydroc...	13C-19-N07	1
Fagron	5-aminolevulinic acid hydroc...	13K27-N02	2

- 111 187 spectra from 742 *Apo-Ident* customers from a total of 31 847 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *5-aminolevulinic acid hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *5-aminolevulinic acid hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	40	0	119 102
Type C	0	58	2	111 187

The substance/substance group *5-aminolevulinic acid hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	96.6667 % (> 91.6667 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *5-aminolevulinic acid hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-threonine	61.18	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *5-aminolevulinic acid hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24733	24733	0.00	86.17
21339	23208	18.85	82.47
23208	23208	0.00	89.03
23403	23208	16.32	75.79
23404	23208	13.84	76.84
23747	23208	3.93	88.97

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Acacia, dried dispersion**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20457-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Acacia, dried dispersion; Acaciae gummi dispersione desiccatum

Special notes

When selecting the *Acacia, dried dispersion* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Acacia, dried dispersion	3	2	10

Second-stage model

For differentiation of the substance/substance group *Acacia, dried dispersion* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Acacia, dried dispersion*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Acacia, dried di...	14141901	21431	120	AR-15-FG-006809-01
Caelo	Acacia, dried di...	15413201	22653	40	AR-17-FG-000844-01
Caelo	Acacia, dried di...	181860	24730	40	20180725*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 3 reference samples from the substance/substance group *Acacia, dried dispersion*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 489 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Acacia, dried dispersion*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Acacia, dried dispersion	162331	22853	40
Caelo	Acacia, dried dispersion	16233105	23443	40
Caelo	Acacia, dried dispersion	16233105	23444	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 9 *Apo-Ident* customers from 11 batches from the substance/substance group *Acacia, dried dispersion*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Acacia, dried dispersion	12138607	1
Caelo	Acacia, dried dispersion	12111301	1
Caelo	Acacia, dried dispersion	16233105	1
Caelo	Acacia, dried dispersion	15413207	1
Caelo	Acacia, dried dispersion	3314A160121	1
Caelo	Acacia, dried dispersion	12138612	1
Caelo	Acacia, dried dispersion	12372302	1
Caelo	Acacia, dried dispersion	11345715	1
Klenk	Acacia, dried dispersion	3314A140121	1
Caelo	Acacia, dried dispersion	15086704	1
Caelo	Acacia, dried dispersion	15413201	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Acacia, dried dispersion* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Acacia, dried dispersion* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	120	0	119 022
Type C	0	9	2	111 236

The substance/substance group *Acacia, dried dispersion* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Acacia, dried dispersion* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
SyrSpend® SF pH4	12.46	—
SyrSpend® SF Alka	14.34	—
Corn starch	16.99	—
Rice starch	17.19	—
Hyaluronic acid sodium salt	22.30	—
Wheat starch	24.21	—
Carmellose sodium (400 / 450 / 500 / 6...	25.45	—
Potato starch	27.57	—
Aciclovir	51.03	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Acacia, dried dispersion* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21431	21431	0.00	11.96
24730	24730	0.00	14.14
22653	22653	0.00	12.24

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at

least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Acetylcysteine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20040-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Acetylcysteine; Acetylcysteinum

Special notes

When selecting the *Acetylcysteine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Acetylcysteine	6	7	25

Second-stage model

For differentiation of the substance/substance group *Acetylcysteine* the following second-stage model is used:

- [Submodel 7](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Acetylcysteine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Acetylcysteine	12299020	21315	40	20121026
Caelo	Acetylcysteine	161398	22469	60	20160520*
Euro OTC	Acetylcysteine	1208026-01	21628	60	20121116
Euro OTC	Acetylcysteine	1510016	22228	60	20151116*
Euro OTC	Acetylcysteine	1610011	22854	40	20161107*
Fagron	Acetylcysteine	15C16-B06-308039	22886	40	20150402

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *Acetylcysteine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 389 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Acetylcysteine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Acetylcysteine	163340	23035	40
Euro OTC	Acetylcysteine	1801037	23956	40
Euro OTC	Acetylcysteine	1809026	24302	40
Euro OTC	Acetylcysteine	1907008	24837	40
Euro OTC	Acetylcysteine	1911003	24981	40
Fagron	Acetylcysteine	18B01-B04-357511	24703	40
Fagron	Acetylcysteine	18K06-B02-363236	25043	40

- 118862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 36 spectra from 29 *Apo-Ident* customers from 26 batches from the substance/substance group *Acetylcysteine*.
- Among them are spectra of independent samples from 25 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Acetylcysteine	12299004	1
Caelo	Acetylcysteine	10230713	1
Caelo	Acetylcysteine	16139802	2
Caelo	Acetylcysteine	1011171701	1
Caelo	Acetylcysteine	18180405	1
Caelo	Acetylcysteine	17357305	1
Caelo	Acetylcysteine	16139808	1
Caelo	Acetylcysteine	12299021	1
Caelo	Acetylcysteine	15114007	1
Caelo	Acetylcysteine	16334006	4
Caelo	Acetylcysteine	15114013	2
Euro OTC	Acetylcysteine	1809026-01	1
Euro OTC	Acetylcysteine	1610011-02	1
Euro OTC	Acetylcysteine	1510016-01	2
Euro OTC	Acetylcysteine	1505011-01	1
Fagron	Acetylcysteine	14C28-B05-292386	1
Fagron	Acetylcysteine	13A22N07	1
Farmalabor	Acetylcysteine	P1701913-003	1
Gehe	Acetylcysteine	16139813	1
Caelo	Acetylcysteine	12299027	1
Caelo	Acetylcysteine	130702601	1
Euro OTC	Acetylcysteine	120802601	2
Euro OTC	Acetylcysteine	12299010	1
phar	Acetylcysteine	1610011-02	1
Phoenix 06.06.2014	Acetylcysteine	1208026-01	1
Phoenix goettin	Acetylcysteine	1208026-01	1

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Supplier	Substance	Batch	Spectra
Phönix	Acetylcysteine	1208026	1
Euro OTC	Acetylcysteine	180103701	1
Sanacorp 07.03.2016 10,...	Acetylcysteine	15114007	1

- 111 211 spectra from 742 *Apo-Ident* customers from a total of 31 865 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Acetylcysteine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Acetylcysteine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	280	0	118 862
Type C	0	36	0	111 211

The substance/substance group *Acetylcysteine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 83.3333 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Acetylcysteine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Folic acid hydrate	34.57	447.98
Bismuth gallath, basic	47.23	867.24

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Acetylcysteine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21315	22469	9.56	67.50
21628	22469	3.07	59.64
22228	22228	0.00	62.34
22469	22469	0.00	60.23
22886	22228	10.06	66.60
22854	22854	0.00	66.44

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Acetylsalicylic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20449-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Acetylsalicylic acid; Acidum acetylsalicylicum

Special notes

When selecting the *Acetylsalicylic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Acetylsalicylic acid	7	4	65

Second-stage model

For differentiation of the substance/substance group *Acetylsalicylic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Acetylsalicylic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Acetylsalicylic ...	13297509	21383	40	20131014
Caelo	Acetylsalicylic ...	161316	23064	40	20160825*
Euro OTC	Acetylsalicylic ...	1307024-01	21597	45	20130904
Euro OTC	Acetylsalicylic ...	1407026-01	21637	60	20140801
Euro OTC	Acetylsalicylic ...	1601042	22377	40	20160204*
Euro OTC	Acetylsalicylic ...	1608037	22820	40	20160921*
Fagron	Acetylsalicylic ...	14E02-B04-297099	22949	40	20140515

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 305 spectra of 7 reference samples from the substance/substance group *Acetylsalicylic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 384 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Acetylsalicylic acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Acetylsalicylic acid	173098	23806	40
Euro OTC	Acetylsalicylic acid	1703010	23388	40
Euro OTC	Acetylsalicylic acid	1805004	24120	40
Euro OTC	Acetylsalicylic acid	1805003	24127	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 183 spectra from 119 *Apo-Ident* customers from 66 batches from the substance/substance group *Acetylsalicylic acid*.
- Among them are spectra of independent samples from 65 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Acetylsalicylic acid	KNC2152J13	1
ACM	Acetylsalicylic acid	KNC2077J14	1
Caelo	Acetylsalicylic acid	15334902	4
Alliance Healthcare	Acetylsalicylic acid	18122605	1
Bombastus	Acetylsalicylic acid	17023102	1
Caelo	Acetylsalicylic acid	16131607	2
Caelo	Acetylsalicylic acid	12212219	1
Caelo	Acetylsalicylic acid	11257126	1
Caelo	Acetylsalicylic acid	12212203	1
Caelo	Acetylsalicylic acid	12212223	3
Caelo	Acetylsalicylic acid	12212236	2
Caelo	Acetylsalicylic acid	12212233	1
Caelo	Acetylsalicylic acid	13324109	3
Caelo	Acetylsalicylic acid	13324118	1
Caelo	Acetylsalicylic acid	14250101	1
Caelo	Acetylsalicylic acid	15081301	3
Caelo	Acetylsalicylic acid	15334907	4
Caelo	Acetylsalicylic acid	15081310	1
Caelo	Acetylsalicylic acid	15334914	3
Caelo	Acetylsalicylic acid	17023111	1
Caelo	Acetylsalicylic acid	17023110	13
Caelo	Acetylsalicylic acid	17329204	3
Caelo	Acetylsalicylic acid	18122601	1
Caelo	Acetylsalicylic acid	18122612	7
Caelo	Acetylsalicylic acid	18122615	1
Caelo	Acetylsalicylic acid	18108306	2
Caelo	Acetylsalicylic acid	13297511	1
Caelo	Acetylsalicylic acid	14189603	1
Caelo	Acetylsalicylic acid	15081304	1

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Supplier	Substance	Batch	Spectra
Caelo	Acetylsalicylic acid	17023108	4
Caelo	Acetylsalicylic acid	18122602	6
Caelo	Acetylsalicylic acid	13324116	1
Caelo	Acetylsalicylic acid	15122701	1
Caelo	Acetylsalicylic acid	10099907	1
Caelo	Acetylsalicylic acid	12212230	1
Caelo	Acetylsalicylic acid	13324119	1
Caelo	Acetylsalicylic acid	15081308	2
Caelo	Acetylsalicylic acid	17023102	7
Caelo	Acetylsalicylic acid	18122605	8
Caelo	Acetylsalicylic acid	12212234	2
Caelo	Acetylsalicylic acid	15334917	3
Caelo	Acetylsalicylic acid	19116604	4
Caelo	Acetylsalicylic acid	13324105	1
Caelo	Acetylsalicylic acid	15334910	1
Caelo	Acetylsalicylic acid	1703010-02	1
Caesar & Loretz GmbH	Acetylsalicylic acid	15334914	1
Caesar & Loretz GmbH	Acetylsalicylic acid	15334917	1
Caesar & Loretz GmbH	Acetylsalicylic acid	18122612	1
Caesar & Loretz GmbH	Acetylsalicylic acid	19116604	1
Calo	Acetylsalicylic acid	15334902	1
EuRho	Acetylsalicylic acid	1307024-01	2
EuRho	Acetylsalicylic acid	1407025-01	1
EuRo Gehe	Acetylsalicylic acid	147026-01	1
Euro OTC	Acetylsalicylic acid	1011015-01	1
Euro OTC	Acetylsalicylic acid	20030611-1	1
Euro OTC	Acetylsalicylic acid	1212005-01	3
Euro OTC	Acetylsalicylic acid	1805004-01	1
Euro OTC	Acetylsalicylic acid	1601042-02	1
Euro OTC	Acetylsalicylic acid	1407025	1
Euro OTC	Acetylsalicylic acid	1407025-01	17
Euro OTC	Acetylsalicylic acid	1501046-01	4
Euro OTC	Acetylsalicylic acid	815A-01012	1
Fagron	Acetylsalicylic acid	14B10-B02-296841	1
Gehe	Acetylsalicylic acid	10365302	1
Gehe	Acetylsalicylic acid	18122602	1
GEHE	Acetylsalicylic acid	17023110	1
Caelo	Acetylsalicylic acid	13324101	1
Caelo	Acetylsalicylic acid	301115	1
Caelo	Acetylsalicylic acid	1110417	1
Caelo	Acetylsalicylic acid	1061117/17023107	1
L12	Acetylsalicylic acid	15334917	1
Noweda	Acetylsalicylic acid	10040403	1
Bombastus	Acetylsalicylic acid	1212005-01	1
Caelo	Acetylsalicylic acid	17023107	8
Phoenix	Acetylsalicylic acid	13324107	1
Phoenix	Acetylsalicylic acid	19116604	1
Phoenix/Cealo	Acetylsalicylic acid	17356301	1
Phönix	Acetylsalicylic acid	13324114	1
Euro OTC	Acetylsalicylic acid	1107007-01	1
sanacorp	Acetylsalicylic acid	14250101	1
Sanacorp	Acetylsalicylic acid	1307024-01	1
Sanacorp	Acetylsalicylic acid	13324109	1
Sanacorp	Acetylsalicylic acid	17329204	1
Euro OTC	Acetylsalicylic acid	1307024-01	6

- 111 064 spectra from 742 *Apo-Ident* customers from a total of 31 827 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are docu-

mented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Acetylsalicylic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Acetylsalicylic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	305	0	110 384
Type B	0	160	0	118 982
Type C	0	171	12	111 064

The substance/substance group *Acetylsalicylic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0328 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	93.4426 % (> 91.8033 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Acetylsalicylic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	37.87	—
Indometacin	64.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Acetylsalicylic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21383	22377	7.48	61.57
21597	22377	10.01	60.27
21637	22820	12.67	60.67
22377	22377	0.00	58.23
22820	22820	0.00	57.92
22949	22377	7.48	52.49
23064	23064	0.00	62.92

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Aciclovir**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21677-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Aciclovir; Aciclovirum

Special notes

When selecting the *Aciclovir* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Aciclovir	4	2	10

Second-stage model

For differentiation of the substance/substance group *Aciclovir* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Aciclovir*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Aciclovir	13B04-B40-294559	21677	60	AR-15-FG-002570-01
Fagron	Aciclovir	13B04-B40-302333	21761	60	20131217
Fagron	Aciclovir	14G07-B05-296462	21831	60	20140728
Fagron	Aciclovir	19I17-F02-366255	25064	40	20191202

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 4 reference samples from the substance/substance group *Aciclovir*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Aciclovir*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Aciclovir	15A15-B10-323362	22938	40
Fagron	Aciclovir	18I18-B04-356027	24570	40
Fagron	Aciclovir	15A15-B10-323362	22939	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 26 spectra from 14 *Apo-Ident* customers from 11 batches from the substance/substance group *Aciclovir*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Aciclovir	18118-B04-355420	1
Fagron	Aciclovir	15AS15-B10-307743	1
Fagron	Aciclovir	14g07-b05-296462	1
Fagron	Aciclovir	146501524	1
Fagron	Aciclovir	15A15-B10-307743	1
Fagron	Aciclovir	15A15-B10-315379	13
Fagron	Aciclovir	15A15-B10-323362	1
Fagron	Aciclovir	16K09-B05-328196	4
Fagron	Aciclovir	17G11-B01-339460	1
Fagron	Aciclovir	18I18-B04-355420	1
Fagron	Aciclovir	17G11-B01-342081	1

- 111 221 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Aciclovir* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Aciclovir* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	120	0	119 022
Type C	0	25	1	111 221

The substance/substance group *Aciclovir* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	96.1538 % (> 84.6154 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Aciclovir* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Arginine	51.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Aciclovir* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21677	21677	0.00	66.29
21761	21677	5.16	68.43
21831	21677	11.81	72.90
25064	21677	6.24	65.15

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Albendazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21596-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Albendazole; Albendazolum

Special notes

When selecting the *Albendazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Albendazole	2	4	7

Second-stage model

For differentiation of the substance/substance group *Albendazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Albendazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Albendazole	12J25-B40-293217	21596	45	AR-15-FG-002571-01
Fagron	Albendazole	16B04-B06-322057	22968	40	20160302

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 85 spectra of 2 reference samples from the substance/substance group *Albendazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 604 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 180 spectra of 4 reference samples from the substance/substance group *Albendazole*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Albendazole	14B05-B41-299704	21730	60
Fagron	Albendazole	14B05-B41-314321	22940	40
Fagron	Albendazole	16B04-B06-329519	23017	40
Fagron	Albendazole	18C21-B04-351586	24578	40

- 118 962 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *Albendazole*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Albendazole	14B05B41-312959	1
Fagron	Albendazole	14B05-B41-305249	1
Fagron	Albendazole	18C21-B04	1
Fagron	Albendazole	14B05-B41-314321	1
Fagron	Albendazole	14B05-B41	1
Fagron	Albendazole	18C21-B04x3	1
Fagron	Albendazole	14b05-b41-314321	1
Fagron	Albendazole	16B04-B06-337998	1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 883 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Albendazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Albendazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	85	0	110 604
Type B	0	180	0	118 962
Type C	0	7	1	111 239

The substance/substance group *Albendazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.9412 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.6667 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Albendazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clonidine hydrochloride	33.98	—
Folic acid hydrate	51.10	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Albendazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22968	21596	20.87	36.41
21596	21596	0.00	32.86

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Alfatradiol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20292-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Alfatradiol; Alfatradiolum

Special notes

When selecting the *Alfatradiol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Alfatradiol	8	4	148

Second-stage model

For differentiation of the substance/substance group *Alfatradiol* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Alfatradiol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Alfatradiol	AP33-16-I-62P2985A	22935	40	20161017
Audor Pharma	Alfatradiol	AP33-18-I-68P3620A	24662	40	20180804
Caelo	Alfatradiol	13201601	21476	120	20130812
Caelo	Alfatradiol	13201601	21477	60	20130812
Caelo	Alfatradiol	191599	24747	40	20190812*
Euro OTC	Alfatradiol	1404001-01	21714	50	1509288
Euro OTC	Alfatradiol	1404001-01	21714SI	60	1509288
Euro OTC	Alfatradiol	1603019	22511	40	20160419*
Euro OTC	Alfatradiol	1603019	22511SI	40	20160419*
Fagron	Alfatradiol	13G19-N06	20940	40	1402683
Fagron	Alfatradiol	15J27-B08-323877	22933	40	20151117
Fagron	Alfatradiol	15J27-B08-323877	22934	40	20151117
Fagron	Alfatradiol	15J27-B08-323877	22934SI	40	20151117

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 650 spectra of 13 reference samples from the substance/substance group *Alfatradiol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 039 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 540 spectra of 13 reference samples from the substance/substance group *Alfatradiol*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Alfatradiol	161804	23354	40
Caelo	Alfatradiol	191598	24738	40
Euro OTC	Alfatradiol	1902020	24621	40
Euro OTC	Alfatradiol	2002017	25118	40
Audor Pharma	Alfatradiol	AP33-16-I-62P2985A	22935SI [†]	40
Audor Pharma	Alfatradiol	AP33-18-I-68P3620A	24662SI [†]	40
Caelo	Alfatradiol	13201601	21477SI [†]	60
Caelo	Alfatradiol	161804	23354SI	40
Caelo	Alfatradiol	191598	24738SI	40
Caelo	Alfatradiol	191599	24747SI [†]	40
Euro OTC	Alfatradiol	1902020	24621SI	40
Euro OTC	Alfatradiol	2002017	25118SI	40
Fagron	Alfatradiol	15J27-B08-323877	22933SI [†]	40

- 118 602 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 390 spectra from 189 *Apo-Ident* customers from 155 batches from the substance/substance group *Alfatradiol*.
- Among them are spectra of independent samples from 149 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance	Alfatradiol	19159803	1
Anzag / Gehe	Alfatradiol	14C20-B02-294943	1
Caelo	Alfatradiol	14C20-B02-294943	2
Fagron	Alfatradiol	12H29-N05	4
Audor Pharma	Alfatradiol	AP5104925A	6
Audor Pharma	Alfatradiol	AP1504015-01A	4
Audor Pharma	Alfatradiol	33-16-I-62P2985A	1
Audor Pharma	Alfatradiol	AP33-16-I-42P2945A	3
Audor Pharma	Alfatradiol	AP21-16-II-14P4511A	8
Audor Pharma	Alfatradiol	AP5100461A	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Audor Pharma	Alfatradiol	APXP103DAA	2
Audor Pharma	Alfatradiol	AP35_17_II_85P3624A	1
Audor Pharma	Alfatradiol	AP33_16_I_62P2985A	1
Audor Pharma	Alfatradiol	AP3316I62P2985A	1
Audor Pharma	Alfatradiol	AP3316I42P2945A	1
Audor Pharma	Alfatradiol	AP35-17-II-85P3624-1A	1
Audor Pharma	Alfatradiol	APXPC0071A	2
Audor Pharma	Alfatradiol	AP1404001-01A	1
Audor Pharma	Alfatradiol	AP1404001-01-A	1
Audor Pharma	Alfatradiol	AP514925A	1
Audor Pharma	Alfatradiol	AP35-17-II-85P3624A	1
Bombastus	Alfatradiol	16G05-B01-335789	1
Caelo	Alfatradiol	11061001	2
Caelo	Alfatradiol	11061005	1
Caelo	Alfatradiol	10319909	1
Caelo	Alfatradiol	12H29-N05	2
Caelo	Alfatradiol	10319904	1
Caelo	Alfatradiol	13130806	2
Caelo	Alfatradiol	511211	1
Caelo	Alfatradiol	5051406	1
Caelo	Alfatradiol	13201605	2
Caelo	Alfatradiol	14037904	3
Caelo	Alfatradiol	14139102	2
Caelo	Alfatradiol	2061504	1
Caelo	Alfatradiol	14130104	1
Caelo	Alfatradiol	15356801	15
Caelo	Alfatradiol	15G07-B01-311881	1
Caelo	Alfatradiol	2830	1
Caelo	Alfatradiol	14139105	2
Caelo	Alfatradiol	14318509	1
Caelo	Alfatradiol	14318512	3
Caelo	Alfatradiol	16087507	1
Caelo	Alfatradiol	14318511	2
Caelo	Alfatradiol	14318514	1
Caelo	Alfatradiol	16087512	5
Caelo	Alfatradiol	19159803	4
Caelo	Alfatradiol	14139103	6
Caelo	Alfatradiol	16087501	6
Caelo	Alfatradiol	18180409	1
Caelo	Alfatradiol	111161607	1
Caelo	Alfatradiol	15356804	6
Caelo	Alfatradiol	19159802	2
Caelo	Alfatradiol	19A24-B03-360709	1
Caelo	Alfatradiol	16180408	3
Caelo	Alfatradiol	14I22-B30-302019	1
Caelo	Alfatradiol	16G05-B01-335789	1
Caelo	Alfatradiol	16087510	2
Caelo	Alfatradiol	14C20-B02-294944	1
Caelo	Alfatradiol	160875105728	1
Caelo	Alfatradiol	5107516	1
Caelo	Alfatradiol	14139104	13
Caelo	Alfatradiol	16087502	7
Caelo	Alfatradiol	4318512	1
Caelo	Alfatradiol	11061004	1
Caelo	Alfatradiol	13130805	5
Caelo	Alfatradiol	16180409	9
Caelo	Alfatradiol	16087511	1
Caelo	Alfatradiol	12164207	6
Caelo	Alfatradiol	13130808	1
Caelo	Alfatradiol	14318502	1

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Supplier	Substance	Batch	Spectra
Caelo	Alfatradiol	11161805	4
Caelo	Alfatradiol	15G07-B01-310227	1
Caesar & Loretz GmbH	Alfatradiol	16180407	1
Caesar & Loretz GmbH	Alfatradiol	16180408	1
Caesar & Loretz GmbH	Alfatradiol	16180413	1
Caesar & Loretz GmbH	Alfatradiol	16087512	1
Caesar & Loretz/Sanacorp	Alfatradiol	16180409	1
Caesar und Loretz GmbH	Alfatradiol	16087502	1
Caesar&Lorenz/Phoenix	Alfatradiol	16087502	1
Caesar&Loretz GmbH/Anzag	Alfatradiol	12164207	1
Caesar/Lorenz	Alfatradiol	11061001	1
carlo	Alfatradiol	10319903	1
Chiracon GmbH	Alfatradiol	AP35-17-II-85P3624	1
Euro OTC	Alfatradiol	AP33-16-1-62P2985A	1
Euro OTC	Alfatradiol	1404001-02	1
Euro OTC	Alfatradiol	160301901	1
Euro OTC	Alfatradiol	15356804	1
Euro OTC	Alfatradiol	121696	1
Euro OTC	Alfatradiol	AP33-16-I-62P2985A	1
Euro OTC	Alfatradiol	16180410	1
Euro OTC	Alfatradiol	16087510	2
Fagron	Alfatradiol	13L30-B32-290742	1
Fagron	Alfatradiol	11B07-N05	1
Fagron	Alfatradiol	XP101UT	1
Fagron	Alfatradiol	13G19-No6	2
Fagron	Alfatradiol	13G19-N06	1
Fagron	Alfatradiol	13G19-N09	1
Fagron	Alfatradiol	13L30B32	1
Fagron	Alfatradiol	13L30B32-290741	1
Fagron	Alfatradiol	14C20-B02-294943	2
Fagron	Alfatradiol	13L30-B32-290739	1
Fagron	Alfatradiol	14G07-B99-294942	1
Fagron	Alfatradiol	14G07-B99	1
Fagron	Alfatradiol	13130b32290742	1
Fagron	Alfatradiol	14722-B30-302018	1
Fagron	Alfatradiol	14C20-B02-294944	1
Fagron	Alfatradiol	14I22-B30	1
Fagron	Alfatradiol	15G07-B01-310228	3
Fagron	Alfatradiol	2735	1
Fagron	Alfatradiol	15J27-B08-314546	1
Fagron	Alfatradiol	15J27-B08-318783	1
Fagron	Alfatradiol	14/22-B30-302017	1
Fagron	Alfatradiol	15G07-B01	1
Fagron	Alfatradiol	16g05-b01-324614	1
Fagron	Alfatradiol	16G05-B01-328254	1
Fagron	Alfatradiol	16G05-B01-326866	1
Fagron	Alfatradiol	16G05-B01-332379	1
Fagron	Alfatradiol	16G05-B01-335789	5
Fagron	Alfatradiol	18C23-B05	2
Fagron	Alfatradiol	9011904	1
Fagron	Alfatradiol	17G03-B11-341399	1
Fagron	Alfatradiol	18C23-B05-356316	1
Fagron	Alfatradiol	11k25-N01	1
Fagron	Alfatradiol	16G05-B01-334055	2
Fagron	Alfatradiol	11G22-N11	2
Fagron	Alfatradiol	11D07-N19	1
Fagron	Alfatradiol	12D19-N03	6
Fagron	Alfatradiol	17G03-B11-345093	2
Fagron	Alfatradiol	15G07-B01-311881	1
Fagron	Alfatradiol	5102432	1

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Supplier	Substance	Batch	Spectra
Fagron	Alfatradiol	14G07-B99-294945	4
Fagron	Alfatradiol	17G03-B11-346962	1
Fagron	Alfatradiol	18C23-B05-352724	1
Fagron	Alfatradiol	16G05-B01-324614	1
Fagron	Alfatradiol	16G05-B01-337352	1
Fagron	Alfatradiol	12L19-N08	7
Fagron	Alfatradiol	324614	1
Fagron	Alfatradiol	13L30-B32	2
Fagron	Alfatradiol	15G07-B01-310229	3
Fagron	Alfatradiol	19A24-B03-360710	1
Fagron	Alfatradiol	12J27-B08-314546	1
Fagron	Alfatradiol	15J27-B08	1
Fagron	Alfatradiol	16G05-801	1
Fagron	Alfatradiol	17G03-B11-341398	2
Fagron	Alfatradiol	11K25-N01	3
Fagron	Alfatradiol	15G07-B01-310227	4
Fagron	Alfatradiol	16G05-B01-332379	1
Fagron	Alfatradiol	16G05-N01-335789	1
Fagron	Alfatradiol	15J27B08318164	1
Fagron	Alfatradiol	15J27-B08-318164	3
Fagron	Alfatradiol	16G05-B01-325108	1
Fagron	Alfatradiol	17G03-B11-348863	1
Fagron	Alfatradiol	5119507	1
Fagron	Alfatradiol	17G03-B11	2
Fagron	Alfatradiol	13201605	1
Fagron	Alfatradiol	15J27-B08-321786	1
Fargon/Kehr	Alfatradiol	16G05-B01-332379	1
Fgron / Alliance Healthc.	Alfatradiol	16G05-B01-328254	1
Gatt-Koller	Alfatradiol	1803210	2
Gatt-Koller	Alfatradiol	180077661	1
Gehe	Alfatradiol	16087501	1
GEHE	Alfatradiol	16087512	1
Fagron	Alfatradiol	18C23-B05-354802	5
Hirsch	Alfatradiol	12L19-N08	2
Kehr	Alfatradiol	18C23-B05-350996	1
Caelo	Alfatradiol	17G03-B11-341398	1
Kwizda	Alfatradiol	529068	1
Noweda	Alfatradiol	16G05-B01-324614	1
Noweda am 10.08.2018	Alfatradiol	16087510	1
Caelo	Alfatradiol	15380001	8
Caelo	Alfatradiol	1536801	1
Phönix	Alfatradiol	APXPC0071A	1
Phönix	Alfatradiol	15356801	1
Caelo	Alfatradiol	16087504	11
Caelo	Alfatradiol	12164201	4
Sanacorp	Alfatradiol	13201605	1
Sanacorp	Alfatradiol	15356804	1
Sanacorp, 39,57EUR, 27.1.17	Alfatradiol	700670-0011	1
Caelo	Alfatradiol	11161807	3
Shandong northwest manu...	Alfatradiol	AEC151211	1
Shandong Northwest Manu...	Alfatradiol	AEC160522	1
Fagron	Alfatradiol	12L19-No8	1
VDL 1.7.14;40.30 euro	Alfatradiol	13G19-N06	1
Audor Pharma	Alfatradiol	AP33-16-I-62P2985A	3
Audor Pharma	Alfatradiol	AP33-18-I-68P3620A	2
Euro OTC	Alfatradiol	1404001-01	2
Fagron	Alfatradiol	13G19-N06	19
Fagron	Alfatradiol		1

- 110 857 spectra from 742 *Apo-Ident* customers from a total of 31 736 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Alfatradiol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Alfatradiol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	650	0	110 039
Type B	0	540	0	118 602
Type C	0	386	4	110 857

The substance/substance group *Alfatradiol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0769 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8889 %)
Type C	100.0000 % (> 99.8899 %)	98.9744 % (> 98.2051 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Alfatradiol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estriol	20.10	65.21
Prednisolon dihydrogen phosphate dinat...	47.09	—
L-glutathione	50.34	—
⋮	⋮	⋮
Progesterone, micronized	>50	156.60
Spironolactone	>50	156.64
Testosterone propionate	>50	176.70
Quinine hydrochloride	>50	200.69
Quinine sulfate	>50	204.32
Pregnenolone	>50	276.06

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Alfatradiol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22934	22511	2.79	26.55
22511	22511	0.00	26.06
20940	20940	0.00	25.35
22935	24747	10.60	31.42
21477	22511	7.65	26.02
24662	22511	8.11	26.64
22933	20940	3.39	27.45
24747	24747	0.00	28.83
21476	22511	5.82	25.99
21714	21714	0.00	20.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Allantoin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20079-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Allantoin; Allantoinum

Special notes

When selecting the *Allantoin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Allantoin	7	3	87

Second-stage model

For differentiation of the substance/substance group *Allantoin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Allantoin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Allantoin	162289	22756	40	20160815*
Caelo	Allantoin	172346	23629	40	20171019*
Caelo	Allantoin	172346	23635	40	20171019*
Euro OTC	Allantoin	1406011-01	21625	60	20140718
Euro OTC	Allantoin	1609012	22750	40	20161006*
Euro OTC	Allantoin	1609012-01	22810	40	20161006
Euro OTC	Allantoin	1406011-04	24095	40	20170213
Fagron	Allantoin	13I03-B05	21216	40	20130927

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 8 reference samples from the substance/substance group *Allantoin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 349 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Allantoin*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Allantoin	181586	24235	40
Caelo	Allantoin	191828	24894	40
Euro OTC	Allantoin	1811006	24344	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 329 spectra from 144 *Apo-Ident* customers from 90 batches from the substance/substance group *Allantoin*.
- Among them are spectra of independent samples from 87 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Allantoin	1609012-01	1
Caelo	Allantoin	15220006	14
Caelo	Allantoin	18158604	2
Anzag;18.03.15;2,76EUR	Allantoin	14247602	1
Caelo	Allantoin	20071202	1
Caelo	Allantoin	81542358	2
Caelo	Allantoin	140512	1
Caelo	Allantoin	20140612-15	1
Caelo	Allantoin	12251501	4
Caelo	Allantoin	11247511	2
Caelo	Allantoin	12251502	2
Caelo	Allantoin	2713431	1
Caelo	Allantoin	1113E-01087	1
Caelo	Allantoin	12251510	9
Caelo	Allantoin	1251505	1
Caelo	Allantoin	10318305	1
Caelo	Allantoin	10064012	1
Caelo	Allantoin	12374404	2
Caelo	Allantoin	12374407	4
Caelo	Allantoin	5051402	1
Caelo	Allantoin	15220004	1
Caelo	Allantoin	15220008	1
Caelo	Allantoin	15220008	8
Caelo	Allantoin	4247602	1
Caelo	Allantoin	15275302	1
Caelo	Allantoin	15220012	11
Caelo	Allantoin	152200012	1
Caelo	Allantoin	16228903	10
Caelo	Allantoin	1522000	1
Caelo	Allantoin	28101702	1

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Supplier	Substance	Batch	Spectra
Caelo	Allantoin	16228906	12
Caelo	Allantoin	121127	1
Caelo	Allantoin	16228904	1
Caelo	Allantoin	17355903	6
Caelo	Allantoin	18158602	1
Caelo	Allantoin	18158605	1
Caelo	Allantoin	10064008	4
Caelo	Allantoin	2713448	1
Caelo	Allantoin	12374418	2
Caelo	Allantoin	15220005	2
Caelo	Allantoin	11247504	5
Caelo	Allantoin	12374403	8
Caelo	Allantoin	14247609	8
Caelo	Allantoin	12374401	1
Caelo	Allantoin	12251511	1
Caelo	Allantoin	10064015	1
Caelo	Allantoin	15275305	2
Caelo	Allantoin	10318313	1
Caelo	Allantoin	12374414	8
Caelo	Allantoin	12374422	8
Caelo	Allantoin	12374415	10
Caelo	Allantoin	15275312	8
Caelo	Allantoin	12374408	1
Caelo	Allantoin	16228914	2
Caelo	Allantoin	1406011-05	1
Caelo	Allantoin	15220011	2
Caelo	Allantoin	2264594	1
Caelo	Allantoin	10318312	1
Caelo	Allantoin	15220010	3
Caelo	Allantoin	15275304	2
Caelo	Allantoin	16228915	21
Caelo	Allantoin	11247510	2
Caelo	Allantoin	1225101	1
Caelo	Allantoin	12374409	15
Caelo	Allantoin	12374417	1
Caelo	Allantoin	12374423	2
Caelo	Allantoin	14247602	6
Caelo	Allantoin	15220007	4
Caesar & Loretz GmbH	Allantoin	12251505	1
Caesar & Loretz GmbH	Allantoin	12251510	1
Caesar & Loretz GmbH	Allantoin	12374403	1
Caesar & Loretz GmbH	Allantoin	12374409	1
Caesar & Loretz GmbH	Allantoin	12374415	1
Caesar & Loretz GmbH	Allantoin	14247602	1
Caesar & Loretz GmbH	Allantoin	12374416	1
Caesar & Loretz GmbH	Allantoin	18158602	1
Caesar & Loretz GmbH	Allantoin	18158604	1
Caesar&Loretz GmbH	Allantoin	12374409	1
celo/Jenne	Allantoin	12374403	1
DSM Nutritional Prod./ ...	Allantoin	12251505	1
EuRho	Allantoin	1406011-04	1
EuRho / Phoenix	Allantoin	1406011-03	1
Euro OTC	Allantoin	1401046-01	3
Euro OTC	Allantoin	140601103	1
Euro OTC	Allantoin	1609012-03	1
Euro OTC	Allantoin	1406011	2
Euro OTC	Allantoin	15220008	2
Euro OTC	Allantoin	1406011-02	2
Euro OTC	Allantoin	140104601	1
Euro OTC	Allantoin	1609012-02	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Allantoin	1811006-01	1
Euro OTC	Allantoin	160901202	1
Euro OTC	Allantoin	1406011-05	1
Fagron	Allantoin	12C30-N04	1
Fagron	Allantoin	11J11-N11	3
Fagron	Allantoin	12B09-N09	1
Fagron	Allantoin	13I03-B05-289430	1
Fagron	Allantoin	5011E-01087	1
Fagron	Allantoin	13A21-N07	3
Fagron	Allantoin	13G16-N07	6
Fargron/AHD	Allantoin	13G16-N07	1
Gehe	Allantoin	12251510	1
Gehe	Allantoin	14247603	1
Ichthyol-Gesellschaft	Allantoin	16228915	1
Kehr	Allantoin	15220008	1
Krieger/Hedinger	Allantoin	15220006	1
Merck	Allantoin	1609012-01	1
Noweda	Allantoin	16228915	1
Phoenix 08.10.14	Allantoin	1401046-01	1
Caelo	Allantoin	12251505	7
Sanacorp	Allantoin	12251501	1
Sanacorp	Allantoin	12251510	1
Sanacorp	Allantoin	12374409	2
Sanacorp	Allantoin	12374422	1
Spinnrad	Allantoin	1217503012	1
VDL 17.10.14	Allantoin	12374415	1
Euro OTC	Allantoin	1406011-01	7
Euro OTC	Allantoin	1609012-01	7
Euro OTC	Allantoin	1406011-04	1

- 110918 spectra from 742 *Apo-Ident* customers from a total of 31 801 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Allantoin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Allantoin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	120	0	119 022
Type C	0	324	5	110 918

The substance/substance group *Allantoin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	98.4802 % (> 97.5684 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Allantoin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxalic acid	32.34	—
Levothyroxin sodium	39.22	—
Bismuth gallath, basic	61.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Allantoin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21216	22756	4.49	33.63
21625	22750	6.47	32.34
22750	22750	0.00	34.20
22756	22756	0.00	33.60
22810	22750	3.09	33.44
23629	23629	0.00	32.98
23635	23635	0.00	32.35
24095	22750	2.70	34.09

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Allopurinol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22243-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Allopurinol; Allopurinolum

Special notes

When selecting the *Allopurinol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Allopurinol	2	2	2

Second-stage model

For differentiation of the substance/substance group *Allopurinol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Allopurinol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Allopurinol	14E15-B05-307746	22243	60	AR-16-FG-004367-01
Fagron	Allopurinol	14E15-B05-315557	22345	60	20140611
Fagron	Allopurinol	14E15-B05-307746	22836	40	20140611

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Allopurinol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 529 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Allopurinol*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Allopurinol	14E15-B05-330859	23523	40
Fagron	Allopurinol	18E23-B02-357777	24577	40
Fagron	Allopurinol	14E15-B05-330859	23526	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 15 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Allopurinol*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Allopurinol	14E15-B08	1
Fagron	Allopurinol	14E15-B05-320787	1
Fagron	Allopurinol	14E15-B05-315557	13

- 111 232 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Allopurinol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Allopurinol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	120	0	119 022
Type C	0	15	0	111 232

The substance/substance group *Allopurinol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Allopurinol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Miconazole nitrate	72.48	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Allopurinol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22243	22243	0.00	76.76
22345	22243	1.06	76.19
22836	22243	2.87	76.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **alpha-tocopheryl acetate dry concentrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20433-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

alpha-tocopheryl acetate dry concentrate; alpha-Tocopherolum aceticum siccatum

Special notes

When selecting the *alpha-tocopheryl acetate dry concentrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
alpha-tocopheryl acetate dry concentrate	7	3	12

Second-stage model

For differentiation of the substance/substance group *alpha-tocopheryl acetate dry concentrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *alpha-tocopheryl acetate dry concentrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	alpha-tocopheryl...	1110021-02	20907	40	20120104
Euro OTC	alpha-tocopheryl...	1305032-01	21680	60	AR-15-FG-001194-01
Euro OTC	alpha-tocopheryl...	1507001	21842	60	20130708*
Euro OTC	alpha-tocopheryl...	1603046	22543	40	20160429*
Euro OTC	alpha-tocopheryl...	1907033	24841	40	20190820*
Fagron	alpha-tocopheryl...	13H30-B02-287169	21609	60	AR-15-FG-006388-01
Fagron	alpha-tocopheryl...	14B03-B04-295113	21959	60	20140224

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 7 reference samples from the substance/substance group *alpha-tocopheryl acetate dry concentrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *alpha-tocopheryl acetate dry concentrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	alpha-tocopheryl acetate dry...	1705003	23424	40
Euro OTC	alpha-tocopheryl acetate dry...	1810024	24309	40
Fagron	alpha-tocopheryl acetate dry...	16H30-B05-326792	22948	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 20 spectra from 9 *Apo-Ident* customers from 14 batches from the substance/substance group *alpha-tocopheryl acetate dry concentrate*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	alpha-tocopheryl acetate dry...	1507001-02	1
Caelo	alpha-tocopheryl acetate dry...	1603046-02	2
Caelo	alpha-tocopheryl acetate dry...	1705003-01	1
EuRho	alpha-tocopheryl acetate dry...	1810024-01	1
Euro OTC	alpha-tocopheryl acetate dry...	1603046-02	1
Euro OTC	alpha-tocopheryl acetate dry...	160304602	1
Euro OTC	alpha-tocopheryl acetate dry...	170500301	1
Euro OTC	alpha-tocopheryl acetate dry...	181002401	1
Euro OTC	alpha-tocopheryl acetate dry...	1705003-04	1
Euro/Sanacorp	alpha-tocopheryl acetate dry...	150700101	1
Fagron	alpha-tocopheryl acetate dry...	16H30-B05-326792	1
Kehr	alpha-tocopheryl acetate dry...	1705003-03	2
Sanacorp	alpha-tocopheryl acetate dry...	1705003-03	1
Euro OTC	alpha-tocopheryl acetate dry...	1507001-01	2
Euro OTC	alpha-tocopheryl acetate dry...	1110021-02	2
Fagron	alpha-tocopheryl acetate dry...	13H30-B02-287169	1

- 111 227 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *alpha-tocopheryl acetate dry concentrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-*

Ident. For this purpose, all relevant spectra of the various substances were compared with *alpha-tocopheryl acetate dry concentrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	120	0	119 022
Type C	0	20	0	111 227

The substance/substance group *alpha-tocopheryl acetate dry concentrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 70.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *alpha-tocopheryl acetate dry concentrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	33.40	—
Hydrocortisone	34.90	—
Nystatin	39.87	—
Bacitracin	47.26	—
Escin, water-soluble	47.40	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *alpha-tocopheryl acetate dry concentrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20907	21680	3.89	36.55
21959	21680	5.14	36.30
24841	24841	0.00	40.06
21609	21609	0.00	38.11
21680	21680	0.00	36.69
21842	21842	0.00	37.93
22543	22543	0.00	37.83

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ambroxol hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20742-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ambroxol hydrochloride; Ambroxoli hydrochloridum

Special notes

When selecting the *Ambroxol hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ambroxol hydrochloride	10	9	65

Second-stage model

For differentiation of the substance/substance group *Ambroxol hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ambroxol hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ambroxol hydroch...	161996	22636	40	20160810*
Caelo	Ambroxol hydroch...	171582	23344	40	20170607*
Euro OTC	Ambroxol hydroch...	11110008-01	20742	40	1401146
Euro OTC	Ambroxol hydroch...	1311032-01	21244	40	20131219
Euro OTC	Ambroxol hydroch...	1509032	21942	60	20151027*
Euro OTC	Ambroxol hydroch...	1601008	22298	60	20160119*
Euro OTC	Ambroxol hydroch...	1602015	22347	60	20160217*
Euro OTC	Ambroxol hydroch...	1604035	22550	40	20160428*
Fagron	Ambroxol hydroch...	13I24-N02	21230	40	20131017
Fagron	Ambroxol hydroch...	19E01-B02-361735	24821	40	20190606

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 10 reference samples from the substance/substance group *Ambroxol hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 229 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 360 spectra of 9 reference samples from the substance/substance group *Ambroxol hydrochloride*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ambroxol hydrochloride	172860	23801	40
Caelo	Ambroxol hydrochloride	190618	24524	40
Euro OTC	Ambroxol hydrochloride	1609002	22800	40
Euro OTC	Ambroxol hydrochloride	1702004	23155	40
Euro OTC	Ambroxol hydrochloride	1711021	23894	40
Euro OTC	Ambroxol hydrochloride	1806009	24155	40
Euro OTC	Ambroxol hydrochloride	1811039	24423	40
Euro OTC	Ambroxol hydrochloride	1904001	24623	40
Euro OTC	Ambroxol hydrochloride	1911002	24969	40

- 118782 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 268 spectra from 129 *Apo-Ident* customers from 66 batches from the substance/substance group *Ambroxol hydrochloride*.
- Among them are spectra of independent samples from 65 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag	Ambroxol hydrochloride	15G15-B01-316109	1
Caelo	Ambroxol hydrochloride	16199602	1
Caelo	Ambroxol hydrochloride	1609002-02	1
Caelo	Ambroxol hydrochloride	27101707	1
Caelo	Ambroxol hydrochloride	1702004-02	4
Caelo	Ambroxol hydrochloride	17158201	1
Caelo	Ambroxol hydrochloride	18013208	2
Caelo	Ambroxol hydrochloride	171102101	1
Caelo	Ambroxol hydrochloride	18013211	10
Caelo	Ambroxol hydrochloride	26011902	1
Caelo	Ambroxol hydrochloride	18013219	3
Caelo	Ambroxol hydrochloride	2021904	1
Caelo	Ambroxol hydrochloride	19061809	5
Caelo	Ambroxol hydrochloride	19061815	3
Caelo	Ambroxol hydrochloride	170522AH/16309201	1
Caelo	Ambroxol hydrochloride	16199603	2
Caelo	Ambroxol hydrochloride	17002902	1
Caelo	Ambroxol hydrochloride	16309201	1
Caelo	Ambroxol hydrochloride	1602015-02	1
Caelo	Ambroxol hydrochloride	1801306	1
Caelo	Ambroxol hydrochloride	17158202	2
Caelo	Ambroxol hydrochloride	18013205	7

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Supplier	Substance	Batch	Spectra
Caelo	Ambroxol hydrochloride	1711021-02	2
Caelo	Ambroxol hydrochloride	17158204	1
Caelo	Ambroxol hydrochloride	1811039-01	1
Caelo	Ambroxol hydrochloride	17002904	1
Caelo	Ambroxol hydrochloride	18013201	5
Caelo	Ambroxol hydrochloride	19061804	8
Caelo	Ambroxol hydrochloride	17286001	4
Caelo/Gehe	Ambroxol hydrochloride	1702004-02	2
Caesar & Loretz GmbH	Ambroxol hydrochloride	18013205	1
Caesar & Loretz GmbH	Ambroxol hydrochloride	18013219	1
Caesar & Loretz GmbH	Ambroxol hydrochloride	17286001	1
Caesar & Loretz GmbH	Ambroxol hydrochloride	19061804	1
Caesar & Loretz GmbH/G	Ambroxol hydrochloride	19061809	3
Cealo/Gehe	Ambroxol hydrochloride	171158204	1
Chem & Pharma	Ambroxol hydrochloride	AXL0361201310	1
E-plus	Ambroxol hydrochloride	1711021-02	1
EuRho	Ambroxol hydrochloride	1602015-02	2
EuRho/Fiebig	Ambroxol hydrochloride	1811039-01	1
Eurho/Phoenix	Ambroxol hydrochloride	190400101	1
Euro OTC	Ambroxol hydrochloride	AXL0592201803	2
Euro OTC	Ambroxol hydrochloride	171102101	1
Euro OTC	Ambroxol hydrochloride	1509032-01	1
Euro OTC	Ambroxol hydrochloride	1602015-02	1
Euro OTC	Ambroxol hydrochloride	1609002-02	14
Euro OTC	Ambroxol hydrochloride	3111805	1
Euro OTC	Ambroxol hydrochloride	1806009	1
Euro OTC	Ambroxol hydrochloride	181103901	2
Euro OTC	Ambroxol hydrochloride	190400101	1
Euro OTC	Ambroxol hydrochloride	160215-02	1
Euro OTC	Ambroxol hydrochloride	1702004-01	10
Euro OTC	Ambroxol hydrochloride	170192	1
Euro OTC	Ambroxol hydrochloride	27061702	1
Euro OTC	Ambroxol hydrochloride	170200402	1
Euro OTC	Ambroxol hydrochloride	1711021-01	13
Euro OTC	Ambroxol hydrochloride	1811039-01	11
Euro OTC	Ambroxol hydrochloride	1609002-01	8
Euro OTC	Ambroxol hydrochloride	AXL0601201807	1
Euro OTC	Ambroxol hydrochloride	1711021-02	18
Euro OTC	Ambroxol hydrochloride	2(1904001-01)	1
Euro OTC	Ambroxol hydrochloride	1806009-01	16
Euro OTC	Ambroxol hydrochloride	1702004-02	5
Euro OTC	Ambroxol hydrochloride	1604035-02	8
Euro OTC	Ambroxol hydrochloride	1904001-01	10
Euro OTC	Ambroxol hydrochloride	171102-01	1
Euro OTC	Ambroxol hydrochloride	19040101	1
Euro/Noweda	Ambroxol hydrochloride	1509032-01	1
Euro/Noweda	Ambroxol hydrochloride	181103901	1
Euro OTC	Ambroxol hydrochloride	1604035-01	1
Euro OTC	Ambroxol hydrochloride	1604032-01	1
EuroTOC	Ambroxol hydrochloride	1602015-01	1
Fagron	Ambroxol hydrochloride	12K12-N02	1
Fagron	Ambroxol hydrochloride	1602015-01	1
Fagron	Ambroxol hydrochloride	16G12-B06-326184	1
Gatt-Koller	Ambroxol hydrochloride	180600901	1
Gatt-Koller	Ambroxol hydrochloride	181103901	2
Gehe	Ambroxol hydrochloride	19061804	2
Gehe	Ambroxol hydrochloride	1911002-01	1
GEHE	Ambroxol hydrochloride	1702004-02	1
GEHE	Ambroxol hydrochloride	1711021-01	1
GEHE	Ambroxol hydrochloride	1904001-01	3

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Supplier	Substance	Batch	Spectra
Caelo	Ambroxol hydrochloride	1609002-01	2
Caelo	Ambroxol hydrochloride	19061803	6
Kehr	Ambroxol hydrochloride	18013201	1
Noweda	Ambroxol hydrochloride	17158201	2
Noweda 23.07.2019	Ambroxol hydrochloride	19061804	1
Noweda/EuRo	Ambroxol hydrochloride	1609002-02	1
Euro OTC	Ambroxol hydrochloride	1(1806009-01)	1
Euro OTC	Ambroxol hydrochloride	ax10492201608	1
Phoenix	Ambroxol hydrochloride	1604035-02	1
Phoenix	Ambroxol hydrochloride	3188	1
Phoenix	Ambroxol hydrochloride	3198	1
PHÖNIX	Ambroxol hydrochloride	1702004-01	1
Sanacorp	Ambroxol hydrochloride	170204-02	1
Sanacorp	Ambroxol hydrochloride	1711021-01	2
Sanacorp	Ambroxol hydrochloride	18013219	2
SANACORP	Ambroxol hydrochloride	1811039-01	2
SANACORP	Ambroxol hydrochloride	19061802	1
Sanacorp EURO	Ambroxol hydrochloride	1806009-01	1
Euro OTC	Ambroxol hydrochloride	1311032-01	1

- 110 979 spectra from 742 *Apo-Ident* customers from a total of 31 827 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ambroxol hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ambroxol hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	460	0	110 229
Type B	0	360	0	118 782
Type C	0	264	4	110 979

The substance/substance group *Ambroxol hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8899 %)	98.5075 % (> 97.3881 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ambroxol hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium citrate	41.75	—
Morphine sulfate	44.56	—
Levothyroxin sodium	55.49	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ambroxol hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22550	22550	0.00	44.87
20742	20742	0.00	44.17
21230	20742	4.81	45.24
21244	22550	4.18	44.66
21942	21942	0.00	43.25
22298	22298	0.00	44.18
22347	22347	0.00	44.27
22636	22636	0.00	44.29
23344	23344	0.00	44.64
24821	22550	5.22	45.27

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Amifampridine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20317-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Amifampridine; Amifampridinum

Special notes

When selecting the *Amifampridine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Amifampridine	5	2	29

Second-stage model

For differentiation of the substance/substance group *Amifampridine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Amifampridine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Amifampridine	17251208	24177	40	20171117
Fagron	Amifampridine	13F05-N01	20901	41	20130606
Fagron	Amifampridine	16A22-B04-317264	22321	60	20160204
Inresa	Amifampridine	0631350001	21781	60	8899
Inresa	Amifampridine	33-15-IV-56P2749B	22848	40	20160822

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 241 spectra of 5 reference samples from the substance/substance group *Amifampridine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 448 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Amifampridine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Amifampridine	17J11-B01-340962	23766	40
Inresa	Amifampridine	33-16-I-77P3018	23723	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 62 spectra from 10 *Apo-Ident* customers from 31 batches from the substance/substance group *Amifampridine*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Amifampridine	33-15-IV-56P2749	1
Caelo	Amifampridine	33-15IV-56P2749B	1
Caelo	Amifampridine	17251207	1
Caelo	Amifampridine	17251206	1
Caelo	Amifampridine	17251210	3
Caelo	Amifampridine	14H11-B06-298447	2
Caelo	Amifampridine	19180703	1
Fagron	Amifampridine	11K07-N02	1
Fagron	Amifampridine	11/14-N03	1
Fagron	Amifampridine	13K14-M01	1
Fagron	Amifampridine	13L12-M06	2
Fagron	Amifampridine	14H11-B06	3
Fagron	Amifampridine	15B20-B02	2
Fagron	Amifampridine	16D05-B01-318216	1
Fagron	Amifampridine	16D05-B01	1
Fagron	Amifampridine	16K15-B03-330546	1
Fagron	Amifampridine	13F07-N07	1
Gehe	Amifampridine	13F07-N07	1
Caelo	Amifampridine	13f05-n01	1
Fagron	Amifampridine	13L12-M03	1
inresa	Amifampridine	58010001	1
inresa	Amifampridine	58710001	2
inresa	Amifampridine	580710001	2
inresa	Amifampridine	631350001	1
Inresa	Amifampridine	508670001	1
Inresa	Amifampridine	580710001	9
Inresa	Amifampridine	63150001	1
Inresa	Amifampridine	631350001	3
Inresa	Amifampridine	33-15-IV-56P2749	2
Inresa	Amifampridine	33-15-IV-56P2749B/22	3
Inresa	Amifampridine	33-16-I-77P3018/1307	2
Inresa	Amifampridine	33-16-I-77P3018	3
Inresa	Amifampridine	3316I77P301816022018	1
Inresa Arzneimittel GmbH	Amifampridine	33-16-I-77P3018/1307	1
Inresa	Amifampridine	33-15-IV-56P2749B	3

- 111 185 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Amifampridine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Amifampridine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	241	0	110 448
Type B	0	80	0	119 062
Type C	0	54	8	111 185

The substance/substance group *Amifampridine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5104 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	87.0968 % (> 82.2581 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Amifampridine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	22.24	—
Bismuth gallath, basic	59.54	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Amifampridine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20901	21781	4.00	27.30
21781	21781	0.00	26.86
22321	21781	4.38	26.85
22848	21781	4.53	27.07
24177	21781	6.04	27.44

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Amitriptyline hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22844-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Amitriptyline hydrochloride; Amitriptylini hydrochloridum

Special notes

When selecting the *Amitriptyline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Amitriptyline hydrochloride	4	2	11

Second-stage model

For differentiation of the substance/substance group *Amitriptyline hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Amitriptyline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Amitriptyline hy...	16C31-B01-325540	22844	40	20160425
Fagron	Amitriptyline hy...	18A16-B06-348643	24180	40	1909242
Inresa	Amitriptyline hy...	005669/17112016	22845	40	1705099
Inresa	Amitriptyline hy...	005669/06022017	23078	40	20160524

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Amitriptyline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Amitriptyline hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Amitriptyline hydrochloride	17E11-B02-335098	23528	40
Fagron	Amitriptyline hydrochloride	19C08-B02-362280	24689	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 16 spectra from 6 *Apo-Ident* customers from 13 batches from the substance/substance group *Amitriptyline hydrochloride*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Amitriptyline hydrochloride	2715E-07209	1
Fagron	Amitriptyline hydrochloride	18A16-B06-344853	2
Fagron	Amitriptyline hydrochloride	18A16-B06-348642	2
Fagron	Amitriptyline hydrochloride	18A16-B06-353064	1
Fagron	Amitriptyline hydrochloride	19C08-B02-365574	1
Fagron	Amitriptyline hydrochloride	19C08-B02-362281	1
Fagron	Amitriptyline hydrochloride	19C08-B02-362280	1
Fagron	Amitriptyline hydrochloride	17E11-B02-340187	1
Fagron	Amitriptyline hydrochloride	18A16-B06-353065	2
GEHE	Amitriptyline hydrochloride	17E11-B02	1
SANACORP	Amitriptyline hydrochloride	19C08-B02	1
Euro OTC	Amitriptyline hydrochloride		1
Fagron	Amitriptyline hydrochloride	18A16-B06-348643	1

- 111 231 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Amitriptyline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Amitriptyline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	80	0	119 062
Type C	0	16	0	111 231

The substance/substance group *Amitriptyline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Amitriptyline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Benzydamine hydrochloride	22.04	—
Tetracaine hydrochloride	38.32	—
Diltiazem hydrochloride	48.48	—
Omeprazole	52.04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Amitriptyline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22844	24180	5.46	34.00
22845	22845	0.00	34.70
23078	22845	1.38	34.85
24180	24180	0.00	32.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Amphotericin B**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20933-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Amphotericin B; Amphotericinum B

Special notes

When selecting the *Amphotericin B* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Amphotericin B	4	2	3

Second-stage model

For differentiation of the substance/substance group *Amphotericin B* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Amphotericin B*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Amphotericin B	1305033-02	20933	40	1403224
Euro OTC	Amphotericin B	1512026-01	22813	40	20160121
Fagron	Amphotericin B	13I16-N02	21338	40	1508271
Fagron	Amphotericin B	13I16-N02	21951	60	20130911
Fagron	Amphotericin B	16L06-B04-333234	23530	40	20170103

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Amphotericin B*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Amphotericin B*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Amphotericin B	1803036	24065	40
Euro OTC	Amphotericin B	1903002	24614	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 14 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Amphotericin B*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Amphotericin B	1305033-03	12
Fagron	Amphotericin B	5173	1
Fagron	Amphotericin B	16D05-B04	1

- 111 233 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Amphotericin B* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Amphotericin B* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	14	0	111 233

The substance/substance group *Amphotericin B* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Amphotericin B* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	14.68	—
Nystatin	22.99	—
Methylcobalamin	28.96	—
Calcium citrate tetrahydrate	32.07	—
Cyanocobalamin	32.56	—
Magnesium citrate	35.11	—
Colistin sulfate	35.86	—
Escin, water-soluble	35.90	—
Polymyxin B sulfate	37.31	—
Calcium pantothenate	43.68	—
Ethinylestradiol	45.15	—
Citrulline	47.56	—
Levothyroxin sodium	48.56	—
Minoxidil	49.73	—
Selenium yeast	50.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Amphotericin B* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21338	21338	0.00	17.63
21951	21338	6.10	18.34
22813	20933	6.17	15.55
23530	20933	6.22	15.31
20933	20933	0.00	14.68

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at

least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Arginine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20391-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Arginine; Argininum

Special notes

When selecting the *Arginine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Arginine	6	5	34

Second-stage model

For differentiation of the substance/substance group *Arginine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Arginine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Arginine	1604003	22514	40	20160425*
Euro OTC	Arginine	1608031	22801	40	20160916*
Euro OTC	Arginine	1702014	23154	40	20170316*
Euro OTC	Arginine	2001001	25092	40	20200122*
Fagron	Arginine	13J28-B02	21226	40	AR-15-FG-008045-01
Fagron	Arginine	16H24-B04-335673	23748	40	20161010

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Arginine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 449 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 220 spectra of 5 reference samples from the substance/substance group *Arginine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Arginine	L1405020-01	21712	60
Euro OTC	Arginine	1710010	23774	40
Euro OTC	Arginine	1806010	24154	40
Euro OTC	Arginine	1902024	24478	40
Euro OTC	Arginine	1909005	24856	40

- 118 922 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 56 spectra from 16 *Apo-Ident* customers from 35 batches from the substance/substance group *Arginine*.
- Among them are spectra of independent samples from 34 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Arginine	13J28-B02-290463	1
Caelo	Arginine	14I24-B08-303720	1
Caelo	Arginine	15C10-B03-318785	1
Caelo	Arginine	17G10-B07-347888	1
Euro OTC	Arginine	1105040-01	1
Euro OTC	Arginine	L1206006-01	1
Euro OTC	Arginine	1710010-01	2
Euro OTC	Arginine	1902024-01	1
Euro OTC	Arginine	1604003-01	1
Euro OTC	Arginine	17122746	1
Fagron	Arginine	13031801	1
Fagron	Arginine	13J28-B02-290463	6
Fagron	Arginine	14I24-B-303720	1
Fagron	Arginine	14/24-B08-303901	1
Fagron	Arginine	1424-B08-303720	1
Fagron	Arginine	14092035	2
Fagron	Arginine	16D11-B01-322156	1
Fagron	Arginine	16H24-B04-335674	7
Fagron	Arginine	16H24-B04-334063	1
Fagron	Arginine	17G10-B07-345399	1
Fagron	Arginine	13F14-N02	2
Fagron	Arginine	12C21-N04	1
Fagron	Arginine	16H24-B04-328914	1
Fagron	Arginine	14I24-B08-303901	1
Fagron	Arginine	15C10-B03-318784	1
Fagron	Arginine	16D11-B01-323566	1
Fagron	Arginine	16032361	1
Fagron	Arginine	17G10-B07	1
Fagron	Arginine	14B25-B04	2
Fagron	Arginine	14/24-B08-303720	4
Fagron	Arginine	14062019	1
Fagron	Arginine	15102258	1
Fagron	Arginine	121429	1

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Supplier	Substance	Batch	Spectra
GEHE	Arginine	17G10-B07-341856	2
Phönix	Arginine	L1302006-01	1
Fagron	Arginine	16H24-B04-335673	2

- 111 191 spectra from 742 *Apo-Ident* customers from a total of 31 857 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Arginine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Arginine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	219	1	118 922
Type C	0	56	0	111 191

The substance/substance group *Arginine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	99.5455 % (> 98.1818 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 89.2857 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Arginine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Aciclovir	37.38	—
Trometamol	48.94	—
Oxalic acid	55.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Arginine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22801	22801	0.00	49.95
23154	23154	0.00	49.56
23748	22514	1.92	50.25
25092	25092	0.00	50.87
21226	21226	0.00	51.84
22514	22514	0.00	49.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Arginine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20657-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Arginine hydrochloride; Arginini hydrochloridum

Special notes

When selecting the *Arginine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Arginine hydrochloride	6	3	9

Second-stage model

For differentiation of the substance/substance group *Arginine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Arginine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Arginine hydroch...	L1103042-01	20657	40	20110325
Euro OTC	Arginine hydroch...	L1212009-01	20964	40	1402430
Euro OTC	Arginine hydroch...	1306023-01	21776	60	AR-15-FG-008412-01
Euro OTC	Arginine hydroch...	1603033	22512	40	20160425*
Euro OTC	Arginine hydroch...	1610042	22877	40	20161128*
Euro OTC	Arginine hydroch...	1904014	24628	40	20190509*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Arginine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Arginine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Arginine hydrochloride	1711014	23875	40
Euro OTC	Arginine hydrochloride	1809012	24313	40
Euro OTC	Arginine hydrochloride	1909026	24937	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 17 spectra from 5 *Apo-Ident* customers from 12 batches from the substance/substance group *Arginine hydrochloride*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
EuRho	Arginine hydrochloride	1306023-01	1
Euro OTC	Arginine hydrochloride	L1407040-01	1
Euro OTC	Arginine hydrochloride	L1407040-02	1
Euro OTC	Arginine hydrochloride	L1506023-01	1
Fagron	Arginine hydrochloride	12C20-N08	1
Fagron	Arginine hydrochloride	13J28-B03	2
Fagron	Arginine hydrochloride	13J28-B03-287766	1
Fagron	Arginine hydrochloride	13j28-b03-287768	1
Fagron	Arginine hydrochloride	13J28-B032x	1
Fagron	Arginine hydrochloride	13j28-B03-287768	1
Hirundo Products Vertri...	Arginine hydrochloride	6412784-152	2
Euro OTC	Arginine hydrochloride	L1212009-01	3
Euro OTC	Arginine hydrochloride	1306023-01	1

- 111 230 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Arginine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Arginine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	17	0	111 230

The substance/substance group *Arginine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Arginine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Polymyxin B sulfate	47.31	—
Gentamicin sulfate	47.74	—
Sodium citrate	48.37	—
Levothyroxin sodium	49.42	—
Calcium glycerophosphate	49.60	—
Magnesium citrate	49.79	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Arginine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20657	24628	7.20	47.58
20964	20964	0.00	49.59
21776	21776	0.00	47.86
22512	22512	0.00	48.55
22877	22877	0.00	49.03
24628	24628	0.00	48.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ascorbic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20394-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ascorbic acid; Acidum ascorbinicum

Special notes

When selecting the *Ascorbic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ascorbic acid	9	13	69

Second-stage model

For differentiation of the substance/substance group *Ascorbic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ascorbic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ascorbic acid	12350011	21317	40	20121122
Caelo	Ascorbic acid	163452	23062	40	20170125*
Caelo	Ascorbic acid	171358	23288	40	20170524*
Caelo	Ascorbic acid	171358	23293	40	20170524*
Euro OTC	Ascorbic acid	1607025	22672	40	20160801*
Euro OTC	Ascorbic acid	1605024	22680	40	20160617*
Euro OTC	Ascorbic acid	1609015	22789	40	20161006*
Euro OTC	Ascorbic acid	1612018	22918	40	20170109*
Euro OTC	Ascorbic acid	1911012	24936	40	20191204*
Fagron	Ascorbic acid	13G29-B07	21229	40	1410500

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 10 reference samples from the substance/substance group *Ascorbic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 289 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 520 spectra of 13 reference samples from the substance/substance group *Ascorbic acid*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ascorbic acid	190262	24508	40
Caelo	Ascorbic acid	192143	24893	40
Euro OTC	Ascorbic acid	1703040	23128	40
Euro OTC	Ascorbic acid	1703025	23144	40
Euro OTC	Ascorbic acid	1707005	23553	40
Euro OTC	Ascorbic acid	1708026	23701	40
Euro OTC	Ascorbic acid	1710032	23891	40
Euro OTC	Ascorbic acid	1901044	24462	40
Euro OTC	Ascorbic acid	1903008	24634	40
Euro OTC	Ascorbic acid	1909018	24848	40
Euro OTC	Ascorbic acid	1911013	24975	40
Euro OTC	Ascorbic acid	2002022	25126	40
Fagron	Ascorbic acid	19G18-B03-194674	25041	40

- 118 622 spectra from a total of 2407 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 128 spectra from 90 *Apo-Ident* customers from 71 batches from the substance/substance group *Ascorbic acid*.
- Among them are spectra of independent samples from 68 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Ascorbic acid	KNC1488J14	6
ACM	Ascorbic acid	Knc1035j16	1
ACM	Ascorbic acid	KNC1035J16	2
Caelo	Ascorbic acid	12349909	1
Amos Vital	Ascorbic acid	L1120454	1
Amos Vital GmbH	Ascorbic acid	L1411003	1
Amos Vital GmbH/Allianc...	Ascorbic acid	L1711004	1
Amosvital/Fiebig	Ascorbic acid	L1509002	1
Caelo	Ascorbic acid	2061203	1
Caelo	Ascorbic acid	11208606	1
Caelo	Ascorbic acid	12350003	1
Caelo	Ascorbic acid	22101302	1
Caelo	Ascorbic acid	14123809	2
Caelo	Ascorbic acid	14044701/3	1
Caelo	Ascorbic acid	1071404	1
Caelo	Ascorbic acid	14214403	1
Caelo	Ascorbic acid	15084507	1
Caelo	Ascorbic acid	15359003	2

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Supplier	Substance	Batch	Spectra
Caelo	Ascorbic acid	15300007	7
Caelo	Ascorbic acid	153000	1
Caelo	Ascorbic acid	16345205	4
Caelo	Ascorbic acid	12456	1
Caelo	Ascorbic acid	16345204	1
Caelo	Ascorbic acid	4116E-01016	1
Caelo	Ascorbic acid	123test	1
Caelo	Ascorbic acid	123456	1
Caelo	Ascorbic acid	1234567	1
Caelo	Ascorbic acid	17135803	2
Caelo	Ascorbic acid	19026202	2
Caelo	Ascorbic acid	13341803/3	1
Caelo	Ascorbic acid	17360301	6
Caelo	Ascorbic acid	17360308	3
Caelo	Ascorbic acid	18030501	1
Caelo	Ascorbic acid	18127801	1
Caelo	Ascorbic acid	12272601/1	1
Caelo	Ascorbic acid	15084503	1
Caelo	Ascorbic acid	14123910	1
Caelo	Ascorbic acid	12350005	2
Caelo	Ascorbic acid	16050403	4
Caelo	Ascorbic acid	123Test	1
Caelo	Ascorbic acid	17233201	1
Caelo	Ascorbic acid	18030503	1
Caelo	Ascorbic acid	14123915	1
Caelo	Ascorbic acid	18127805	4
Caelo	Ascorbic acid	15300002	4
Caelo	Ascorbic acid	18127811	2
Caelo	Ascorbic acid	16345202	5
Caesar & Loretz GmbH	Ascorbic acid	11208606	1
Caesar & Loretz GmbH	Ascorbic acid	18127811	2
caleo	Ascorbic acid	16345205	1
canea, gehe	Ascorbic acid	VC1242	2
Cealo/Gehe	Ascorbic acid	17360301	1
EuRho	Ascorbic acid	1710032-01	1
Euro OTC	Ascorbic acid	L60502801	1
Euro OTC	Ascorbic acid	17011404	1
Euro OTC	Ascorbic acid	12061408	1
Euro OTC	Ascorbic acid	10071418	1
Euro OTC	Ascorbic acid	1710032-01	1
Euro OTC	Ascorbic acid	L1202011-02	1
Euro OTC	Ascorbic acid	L1708004	1
Gatt-Koller	Ascorbic acid	1802406	2
Gatt-Koller	Ascorbic acid	18020406	1
Gehe	Ascorbic acid	16345205	1
GEHE	Ascorbic acid	16345205	1
GEHE	Ascorbic acid	18127805	1
Gehe/Gehe	Ascorbic acid	L1505001	1
Gesundform	Ascorbic acid	L1110704	1
Kehr	Ascorbic acid	17360301	1
KÖGL	Ascorbic acid	1900900	1
Euro OTC	Ascorbic acid	28081303	1
Euro OTC	Ascorbic acid	11121302	1
Euro OTC	Ascorbic acid	17041406	1
Phoenix	Ascorbic acid	18127801	2
Phoenix	Ascorbic acid	19026202	1
SANACORP	Ascorbic acid	201401318	1
Taoasis	Ascorbic acid	810049	1
Wepa	Ascorbic acid	261120415	1
Wepa	Ascorbic acid	180316-C01	1

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Supplier	Substance	Batch	Spectra
wepa Apoday	Ascorbic acid	2616110375431	1
Wepa Paulus	Ascorbic acid	11406201	1
Zentiva/Alliance Health...	Ascorbic acid	15300007	1
Caelo	Ascorbic acid	12350011	1
Wep apot	Ascorbic acid		1

- 111 119 spectra from 742 *Apo-Ident* customers from a total of 31 826 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ascorbic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ascorbic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	520	0	118 622
Type C	0	126	2	111 119

The substance/substance group *Ascorbic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8462 %)
Type C	100.0000 % (> 99.8899 %)	98.4375 % (> 96.0938 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ascorbic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carbomers 35000 / 50000	63.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ascorbic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21229	21229	0.00	66.37
21317	21229	2.40	62.71
22672	22672	0.00	69.43
22680	22680	0.00	69.40
22789	22789	0.00	66.27
22918	22918	0.00	67.03
23062	23062	0.00	68.18
23288	23288	0.00	66.78
23293	23293	0.00	69.43
24936	24936	0.00	65.71

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ascorbyl palmitate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21053-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ascorbyl palmitate; Ascorbylis palmitas

Special notes

When selecting the *Ascorbyl palmitate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ascorbyl palmitate	5	2	95

Second-stage model

For differentiation of the substance/substance group *Ascorbyl palmitate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ascorbyl palmitate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ascorbyl palmitate	13K04-N01	21053	40	1403226
Fagron	Ascorbyl palmitate	13C06-B40-291206	21665	60	20140306
Fagron	Ascorbyl palmitate	15F01-B99-309774	21851	60	20150615
Fagron	Ascorbyl palmitate	17E18-B06-335527	23520	40	20170606
Fagron	Ascorbyl palmitate	17E18-B06-335527	23520SI	40	20170606
Fagron	Ascorbyl palmitate	19D25-B04-361254	24665	40	20190517

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Ascorbyl palmitate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Ascorbyl palmitate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ascorbyl palmitate	17H04-B01-338484	23987	40
Fagron	Ascorbyl palmitate	18A10-B03-344364	24098	40
Fagron	Ascorbyl palmitate	17H04-B01-338484	23987SI	40
Fagron	Ascorbyl palmitate	18A10-B03-344364	24098SI	40
Fagron	Ascorbyl palmitate	19D25-B04-361254	24665SI [†]	40

- 118942 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 205 spectra from 110 *Apo-Ident* customers from 106 batches from the substance/substance group *Ascorbyl palmitate*.
- Among them are spectra of independent samples from 94 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
18J22-B03-525911	Ascorbyl palmitate	Fagron	1
Fagron	Ascorbyl palmitate	16/30-B03-329375	1
Fagron	Ascorbyl palmitate	K48951390	1
Bionorica	Ascorbyl palmitate	74736	1
Bionorica	Ascorbyl palmitate	74962	1
Bionorica	Ascorbyl palmitate	82275	1
Bionorica	Ascorbyl palmitate	85532	1
Bionorica ethics	Ascorbyl palmitate	85532	2
Bionorica Ethics	Ascorbyl palmitate	82275	1
Bionorica Ethics/ Noweda	Ascorbyl palmitate	85532	2
Bionorica Ethics/Noweda	Ascorbyl palmitate	82275	2
Bionorica EthicsGmbH/Sa...	Ascorbyl palmitate	74736	1
Bionorica/Noweda	Ascorbyl palmitate	77773	2
Bombastus	Ascorbyl palmitate	525526	1
Caelo	Ascorbyl palmitate	18A10-B03-344364	2
Caelo	Ascorbyl palmitate	17H04-B01-525632	1
Caelo	Ascorbyl palmitate	16810-B04525199	1
Caelo	Ascorbyl palmitate	15F01-B99-525121	1
Caelo	Ascorbyl palmitate	17E18-B06	1
Caelo	Ascorbyl palmitate	16B10-B04-525199	1
Caelo	Ascorbyl palmitate	16B-B04-525283	1
Caelo	Ascorbyl palmitate	16130-B03-525358	2
Caelo	Ascorbyl palmitate	18B12-B09-525721	1
Caelo	Ascorbyl palmitate	16B10-B04324111	1
Caelo	Ascorbyl palmitate	17E18-B06-334914	1
Euro OTC	Ascorbyl palmitate	16I30-B03	1
Fagrin/Noweda	Ascorbyl palmitate	18B12-B09525720	1
Fagron	Ascorbyl palmitate	K45532790	2
Fagron	Ascorbyl palmitate	15f01-b99-309774	1
Fagron	Ascorbyl palmitate	15F01-B99-52063	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Fagron	Ascorbyl palmitate	16B10-B04-525199	2
Fagron	Ascorbyl palmitate	15F01-B99-525063	1
Fagron	Ascorbyl palmitate	16I30-B03-329375	1
Fagron	Ascorbyl palmitate	16I30-B03-332623	5
Fagron	Ascorbyl palmitate	16I30-B03-525426	1
Fagron	Ascorbyl palmitate	10061708	1
Fagron	Ascorbyl palmitate	1630-B03-525489	1
Fagron	Ascorbyl palmitate	17E18-B06-525524	3
Fagron	Ascorbyl palmitate	17E18-B06-336731	1
Fagron	Ascorbyl palmitate	17H04-B01-338484	7
Fagron	Ascorbyl palmitate	17E18-B06-334914	1
Fagron	Ascorbyl palmitate	525426	1
Fagron	Ascorbyl palmitate	525489	1
Fagron	Ascorbyl palmitate	525525	1
Fagron	Ascorbyl palmitate	525524	1
Fagron	Ascorbyl palmitate	17E18-B06-525525	1
Fagron	Ascorbyl palmitate	17E18-B06-525514	1
Fagron	Ascorbyl palmitate	K48951290	1
Fagron	Ascorbyl palmitate	16L30-B03-332623	1
Fagron	Ascorbyl palmitate	17E18-B06-5255225	1
Fagron	Ascorbyl palmitate	17E18-B06-525526	1
Fagron	Ascorbyl palmitate	18A10-B03-525701	4
Fagron	Ascorbyl palmitate	23061810	1
Fagron	Ascorbyl palmitate	18B12-B09-525719	2
Fagron	Ascorbyl palmitate	17H04-B01-525632	1
Fagron	Ascorbyl palmitate	18B12B09525719	1
Fagron	Ascorbyl palmitate	18B12-B09-525836	3
Fagron	Ascorbyl palmitate	18B12-B09-3488670092	1
Fagron	Ascorbyl palmitate	18J22-B03-355582	4
Fagron	Ascorbyl palmitate	18B12-B09	1
Fagron	Ascorbyl palmitate	18J22-B03-525911	1
Fagron	Ascorbyl palmitate	188B12-B09-525721	1
Fagron	Ascorbyl palmitate	18J22-B03-361032	1
Fagron	Ascorbyl palmitate	19D25-B04-361254	1
Fagron	Ascorbyl palmitate	19D25-B04-526038	1
Fagron	Ascorbyl palmitate	19I12-F02-364765	2
Fagron	Ascorbyl palmitate	16I30-B03	3
Fagron	Ascorbyl palmitate	17e18b06334914	1
Fagron	Ascorbyl palmitate	18B12-B09-348867	7
Fagron	Ascorbyl palmitate	17H04-B01-340474	3
Fagron	Ascorbyl palmitate	16I30-B03-525489	1
Fagron	Ascorbyl palmitate	17E18-B06	1
Fagron	Ascorbyl palmitate	19D25-B04-362604	2
Fagron	Ascorbyl palmitate	17H04-B01	1
Fagron	Ascorbyl palmitate	16I30-B03-330625	1
Fagron	Ascorbyl palmitate	16I30-B03-525358	3
Fagron	Ascorbyl palmitate	18J22-B03	1
Fagron	Ascorbyl palmitate	16B10-B04-525283	1
Fagron	Ascorbyl palmitate	18B12-B09-525721	2
Fagron	Ascorbyl palmitate	18B12-B09-525889	1
Fagron	Ascorbyl palmitate	15F01-B99-525122	2
Fagron	Ascorbyl palmitate	18j22-b03-355582	2
Fagron	Ascorbyl palmitate	16I30-B03-326543	1
Fagron	Ascorbyl palmitate	16/30-B03-330625	3
Fagron	Ascorbyl palmitate	18A10-B03-344364	16
Fagron	Ascorbyl palmitate	18B12-B09-525799	1
Fagron	Ascorbyl palmitate	18A10B03344364	1
Fagron	Ascorbyl palmitate	K50642890	2
Fagron	Ascorbyl palmitate	19d25b04361254	1
Fagron	Ascorbyl palmitate	14I03-N01	1

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Supplier	Substance	Batch	Spectra
Fagron	Ascorbyl palmitate	15F01-B99-525121	1
Fagron	Ascorbyl palmitate	16B10-B04-525228	1
Fagron	Ascorbyl palmitate	16I30-B03-525380	2
Fagron	Ascorbyl palmitate	K47747490	1
Fagron	Ascorbyl palmitate	925749	1
Fagron	Ascorbyl palmitate	18J22-B03-357638	2
Fagron	Ascorbyl palmitate	19D25-B04	3
Fagron	Ascorbyl palmitate	17H04B01340474	1
Fagron	Ascorbyl palmitate	18812-B09-525719	1
Fagron	Ascorbyl palmitate	19D25-B04-526062	2
Fagron	Ascorbyl palmitate	18J22-B03-525967	1
Fagron	Ascorbyl palmitate	15F01-B99	3
Fagron	Ascorbyl palmitate	16/30-B03	1
Fagron	Ascorbyl palmitate	18b12-B09-525799	1
Fagron	Ascorbyl palmitate	18A10-B03-344364	1
Fagron	Ascorbyl palmitate	19D25-B04-361254	1
L12	Ascorbyl palmitate	18B12-B09	1
Merck	Ascorbyl palmitate	16130-B03	1
Merck	Ascorbyl palmitate	17E18-B06-334914	1
Noweda 27.12.2019	Ascorbyl palmitate	19D25-B04-526062	1
Noweda_22.01.2020	Ascorbyl palmitate	19D25-B04-526038	1
Fagron	Ascorbyl palmitate	18J22-B03_525967	1
Fagron	Ascorbyl palmitate	19112-F02-526151	1
Phoenix	Ascorbyl palmitate	18J22-B03-357638	1
PHOENIX 30.06.2014	Ascorbyl palmitate	UQ21206229	1
PHÖNIX	Ascorbyl palmitate	18a10-B03-344364	1
Fagron	Ascorbyl palmitate	17e18-b06	2
Phönix/Bionorica	Ascorbyl palmitate	18A10-B03-344364	1
Fagron	Ascorbyl palmitate	18B12-B09-525820	1
Fagron	Ascorbyl palmitate	13C06-B40-291206	2
Fagron	Ascorbyl palmitate		4
Fagron	Ascorbyl palmitate	19D25-B04-361254	7
Fagron	Ascorbyl palmitate	17E18-B06-335527	1

- 111 042 spectra from 742 *Apo-Ident* customers from a total of 31 787 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ascorbyl palmitate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ascorbyl palmitate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	200	0	118 942
Type C	0	197	8	111 042

The substance/substance group *Ascorbyl palmitate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	96.0976 % (> 94.6341 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ascorbyl palmitate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	57.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ascorbyl palmitate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24665	21053	10.52	61.42
21665	21053	17.10	57.34
21851	21053	21.47	57.97
23520	21053	16.61	59.94
21053	21053	0.00	62.29

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Atropine sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20653-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Atropine sulfate; Atropine sulphate; Atropini sulfas

Special notes

When selecting the *Atropine sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Atropine sulfate	6	3	12

Second-stage model

For differentiation of the substance/substance group *Atropine sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Atropine sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Atropine sulfate	11180602	20653	30	1405538
Caelo	Atropine sulfate	13173808	21088	40	1403483
Caelo	Atropine sulfate	13357405	21551	50	1504594
Caelo	Atropine sulfate	14336806	21719	60	1510209
Caelo	Atropine sulfate	14336806	21719SI	60	1510209
Caelo	Atropine sulfate	15301601	21920	60	20150930
Caelo	Atropine sulfate	15301601	21920SI	60	20150930
Fagron	Atropine sulfate	16G20-B06-328437	22932	40	20160823

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 8 reference samples from the substance/substance group *Atropine sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 289 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 270 spectra of 7 reference samples from the substance/substance group *Atropine sulfate*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Atropine sulfate	16326802	22952	40
Caelo	Atropine sulfate	170264	23367	40
Caelo	Atropine sulfate	172732	23682	40
Caelo	Atropine sulfate	16326802	22952SI	40
Caelo	Atropine sulfate	170264	23367SI	40
Caelo	Atropine sulfate	172732	23682SI	30
Fagron	Atropine sulfate	16G20-B06-328437	22932SI [†]	40

- 118 872 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 20 spectra from 16 *Apo-Ident* customers from 13 batches from the substance/substance group *Atropine sulfate*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Atropine sulfate	13173809	1
Caelo	Atropine sulfate	15115201	3
Caelo	Atropine sulfate	16c15b03-319166	1
Caelo	Atropine sulfate	17273202	1
Caelo	Atropine sulfate	13357403	1
Caelo	Atropine sulfate	18276510	1
Caelo	Atropine sulfate	16326802	2
Caelo	Atropine sulfate	18099111	2
Caelo	Atropine sulfate	14336807	1
fargon	Atropine sulfate	13K01-N01	1
Gehe	Atropine sulfate	16326802	1
GEHE	Atropine sulfate	17273202	1
Noweda	Atropine sulfate	12250403	1
Noweda	Atropine sulfate	18276510	1
Phönix	Atropine sulfate	15301607	1
Caelo	Atropine sulfate	13357405	1

- 111 227 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Validation results

The validation runs checked whether the substance/substance group *Atropine sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Atropine sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	270	0	118 872
Type C	0	20	0	111 227

The substance/substance group *Atropine sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.7778 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 70.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Atropine sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	41.58	—
Mometasone furoate, micronized	42.67	—
Griseofulvin	48.62	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Atropine sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20653	20653	0.00	50.73
21088	21088	0.00	48.78
21551	21551	0.00	53.75
22932	21088	9.94	47.23
21719	21719	0.00	37.29
21920	21719	8.46	43.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Bacitracin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20851-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bacitracin; Bacitracinum

Special notes

When selecting the *Bacitracin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Bacitracin	5	3	58

Second-stage model

For differentiation of the substance/substance group *Bacitracin* the following second-stage model is used:

- [Submodel 4](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Bacitracin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Bacitracin	13A-03-N11	20851	40	1401189
Fagron	Bacitracin	14A21-B09-292909	21657	60	1511741
Fagron	Bacitracin	14E23-B03-296243	21686	60	1503715
Fagron	Bacitracin	15C12-B06-309185	21898	60	20150324
Fagron	Bacitracin	15C12-B06-309185	21986	60	9466
Fagron	Bacitracin	16B17-B03-322939	22739	40	20160421

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Bacitracin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 369 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 7 reference samples from the substance/substance group *Bacitracin*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Bacitracin	16I12-B03-334194	23531	40
Fagron	Bacitracin	17L11-B02-343685	23933	40
Fagron	Bacitracin	18K14-B04-358690	24815	40
Fagron	Bacitracin	14A21-B09-292909	21657SI [†]	60
Fagron	Bacitracin	14E23-B03-296243	21686SI [†]	60
Fagron	Bacitracin	15C12-B06-309185	21898SI [†]	60
Fagron	Bacitracin	15C12-B06-309185	21986SI [†]	60

- 118 782 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 123 spectra from 79 *Apo-Ident* customers from 65 batches from the substance/substance group *Bacitracin*.
- Among them are spectra of independent samples from 58 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Bacitracin	17L11-B02-344244	1
Bombastus	Bacitracin	17L11-B02-354799	1
Caelo	Bacitracin	16B17-B03	1
Caelo	Bacitracin	14A21-B09-292908	1
Caelo	Bacitracin	15080605	1
Caelo	Bacitracin	16I12-B03-331152	1
Caelo	Bacitracin	17L11-B02-357635	1
Caelo	Bacitracin	15C12-B06-317782	1
Caelo	Bacitracin	17L11-B02-343685	1
Caelo	Bacitracin	C2280092	1
Caelo	Bacitracin	14E23-B03-296243	2
Euro OTC	Bacitracin	17L11-B02-348461	1
Fagraon	Bacitracin	14E23-B03-303424	1
Fagron	Bacitracin	11J17-N01	2
Fagron	Bacitracin	13A03-N11	1
Fagron	Bacitracin	12G12-N17	1
Fagron	Bacitracin	13B25-B01	1
Fagron	Bacitracin	14A21-B09-290643	2
Fagron	Bacitracin	14A21-B09-290645	2
Fagron	Bacitracin	14A21-B09	2
Fagron	Bacitracin	C2280017	3
Fagron	Bacitracin	14E23-B03-296245	2
Fagron	Bacitracin	28051509	1
Fagron	Bacitracin	31071503	1
Fagron	Bacitracin	14E23-B03-303424	3
Fagron	Bacitracin	14e23-b03-296243	1
Fagron	Bacitracin	14E23B03-303424	1

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Bacitracin	15C12-B06-317782	1
Fagron	Bacitracin	16B17B03325856	1
Fagron	Bacitracin	16I12-B03	2
Fagron	Bacitracin	17L11-B02-343686	1
Fagron	Bacitracin	17L11-802	1
Fagron	Bacitracin	17L11-B02-354799	3
Fagron	Bacitracin	17L11-B02-346531	1
Fagron	Bacitracin	14A21-B09-292908	1
Fagron	Bacitracin	16B17-B03-322891	4
Fagron	Bacitracin	17L11B02348461	1
Fagron	Bacitracin	17L11-B02-346961	1
Fagron	Bacitracin	211531	1
Fagron	Bacitracin	2917M-03314	1
Fagron	Bacitracin	14E23B03303424	1
Fagron	Bacitracin	16I12-B03-329401	1
Fagron	Bacitracin	16I12-B03-334052	3
Fagron	Bacitracin	16I12-B03-335331	3
Fagron	Bacitracin	17L11-B02_357635	1
Fagron	Bacitracin	16/12-B03-331152	1
Fagron	Bacitracin	16/12B03335331	1
Fagron	Bacitracin	17L11B02357635	1
Fagron	Bacitracin	16/12-B03-334052	2
Fagron	Bacitracin	14E23-B03-333424	1
Fagron	Bacitracin	16/12-B03-334701	1
Fagron	Bacitracin	C2280111	1
Fagron	Bacitracin	14E23-B03	3
Fagron	Bacitracin	15C12-B06	1
Fagron	Bacitracin	16B17-B03	2
Fagron	Bacitracin	16b17-b03-322939	1
Fagron	Bacitracin	13C13-N10	1
Fagron	Bacitracin	16/12-B03-329401	2
Fagron	Bacitracin	C2280065	2
Fagron	Bacitracin	17L11-B02-348461	2
Fagron	Bacitracin	13D26-N08	1
Fagron	Bacitracin	1612-B033-334052	1
Fagron	Bacitracin	17L11-B02	4
Fagron	Bacitracin	17L11-B02-35400	1
Fargon/Gehe	Bacitracin	C2280092	1
Fargon/Phönix	Bacitracin	15C12-B06-312975	1
Fragon/Phönix	Bacitracin	16/12-B03-329401	1
Gehe	Bacitracin	C2280065	1
Kehr	Bacitracin	16B17-B03-322891	1
Fagron	Bacitracin	17L11-B02-343685	8
Noweda	Bacitracin	17L11-B02-346961	2
Noweda	Bacitracin	17L11-B02-354800	3
Phönix	Bacitracin	c2280065	1
Phönix Gotha	Bacitracin	C2280010	1
Fagron	Bacitracin	15C12-B06-309185	1
Fagron	Bacitracin	16B17-B03-322939	1
Fagron	Bacitracin	14E23-B03-296243	6
Fagron	Bacitracin		1

- 111 124 spectra from 742 *Apo-Ident* customers from a total of 31 826 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Bacitracin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bacitracin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	354	6	118 782
Type C	0	114	9	111 124

The substance/substance group *Bacitracin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	98.3333 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	92.6829 % (> 90.2439 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bacitracin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methylcobalamin	20.82	106.72
Glycyrrhizic acid	21.22	—
Cyanocobalamin	26.15	71.47
Nystatin	27.91	—
Minoxidil	33.24	—
Magnesium citrate	37.81	—
Calcium citrate tetrahydrate	40.82	214.20
Polymyxin B sulfate	41.73	—
Escin, water-soluble	42.41	—
Prednisone	44.11	—
Prednisolon dihydrogen phosphate dinat. . .	46.90	—
Amphotericin B	47.44	—
Estradiol hemihydrate	47.64	—
Ethinylestradiol	48.60	208.33
L-glutathione	49.32	—
Colistin sulfate	50.26	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Bacitracin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21898	21986	3.19	20.82
21657	21657	0.00	25.84
22739	20851	3.98	21.55
20851	20851	0.00	21.22
21686	21686	0.00	28.38
21986	21986	0.00	22.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Beclometasone dipropionate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21046-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Beclometasone dipropionate; Beclometasoni dipropionas

Special notes

When selecting the *Beclometasone dipropionate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Beclometasone dipropionate	5	2	27

Second-stage model

For differentiation of the substance/substance group *Beclometasone dipropionate* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Beclometasone dipropionate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Beclometasone di. . .	1203022-03	21634	55	1509281
Euro OTC	Beclometasone di. . .	1203022-03	21995	60	20120424
Euro OTC	Beclometasone di. . .	1502032	22989	40	20150327*
Euro OTC	Beclometasone di. . .	1502032	22989SI	30	20150327*
Euro OTC	Beclometasone di. . .	1502032	24869	40	20190828*
Fagron	Beclometasone di. . .	13I05-N03	21046	60	1511689
Fagron	Beclometasone di. . .	13E02-B40-293328	21554	40	20140508
Fagron	Beclometasone di. . .	13E02-B40-296353	21977	60	20140508
Fagron	Beclometasone di. . .	13E02-B40-296353	21977SI	29	20140508

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 414 spectra of 9 reference samples from the substance/substance group *Beclometasone dipropionate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 275 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 189 spectra of 7 reference samples from the substance/substance group *Beclometasone dipropionate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Beclometasone dipropionate	15F29-B09-314376	23104	40
Fagron	Beclometasone dipropionate	16B16-B03-342082	23930	40
Euro OTC	Beclometasone dipropionate	1203022-03	21634 [†]	5
Euro OTC	Beclometasone dipropionate	1203022-03	21995SI [†]	28
Euro OTC	Beclometasone dipropionate	1502032	24869SI [†]	31
Fagron	Beclometasone dipropionate	15F29-B09-314376	23104SI	20
Fagron	Beclometasone dipropionate	16B16-B03-342082	23930SI	25

- 118 953 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 52 spectra from 20 *Apo-Ident* customers from 31 batches from the substance/substance group *Beclometasone dipropionate*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Beclometasone dipropionate	13E02-B40-293326	1
Euro OTC	Beclometasone dipropionate	1502032-02	3
Euro OTC	Beclometasone dipropionate	18041820	1
Euro OTC	Beclometasone dipropionate	1502032-03	2
Euro OTC	Beclometasone dipropionate	1203022-01	2
Euro OTC	Beclometasone dipropionate	1502032-01	1
Fagro/Noweda	Beclometasone dipropionate	14D04-B04-302335	1
Fagron	Beclometasone dipropionate	11L01-N03	1
Fagron	Beclometasone dipropionate	12D12-N03	4
Fagron	Beclometasone dipropionate	11F28-N02	2
Fagron	Beclometasone dipropionate	12G04-N11	3
Fagron	Beclometasone dipropionate	13I05N03	1
Fagron	Beclometasone dipropionate	13/05-N03	1
Fagron	Beclometasone dipropionate	13E02-B40-296354	2
Fagron	Beclometasone dipropionate	13/05-N03	1
Fagron	Beclometasone dipropionate	14D04-B04-302336	3
Fagron	Beclometasone dipropionate	C0783/112020	1
Fagron	Beclometasone dipropionate	14D04-B04302336	1
Fagron	Beclometasone dipropionate	16B16-B03-322517	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Fagron	Beclometasone dipropionate	16B16-B03-342082	1
Fagron	Beclometasone dipropionate	15F29-B09-314376	1
Fagron	Beclometasone dipropionate	18C05-B01-347367	1
Fagron	Beclometasone dipropionate	14D04-B04-302335	1
Fagron	Beclometasone dipropionate	16B16-B03-318877	1
Fagron	Beclometasone dipropionate	13E02-B40-293327	4
Fagron	Beclometasone dipropionate	13E02-B40	1
fragon	Beclometasone dipropionate	700721-0004	1
Euro OTC	Beclometasone dipropionate	C0783111020	1
Euro OTC	Beclometasone dipropionate	1203022-03	1
Fagron	Beclometasone dipropionate	13I05-N03	3
Fagron	Beclometasone dipropionate	13E02-B40-293328	2
Fagron	Beclometasone dipropionate	13E02-B40-296353	1

- 111 195 spectra from 742 *Apo-Ident* customers from a total of 31 860 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Beclometasone dipropionate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Beclometasone dipropionate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	414	0	110 275
Type B	0	189	0	118 953
Type C	0	51	1	111 195

The substance/substance group *Beclometasone dipropionate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5507 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.8254 %)
Type C	100.0000 % (> 99.8899 %)	98.0769 % (> 92.3077 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Beclometasone dipropionate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clobetasol propionate	18.24	64.90
Betamethasone dipropionate, micronized	28.46	34.52
Oxybutynin hydrochloride	40.00	97.71
Dexamethasone acetate	42.56	—
Oxycodone hydrochloride	48.95	—
⋮	⋮	⋮
Gentamicin sulfate	>50	227.18
Sodium citrate	>50	402.76
Sodium benzoate	>50	665.39

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Beclometasone dipropionate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21046	21046	0.00	28.99
21634	21634	0.00	28.09
21977	21634	2.47	27.20
21554	22989	2.00	27.67
24869	24869	0.00	26.96
21995	21634	2.11	27.27
22989	22989	0.00	27.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Benzocaine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20211-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Benzocaine; Benzocainum

Special notes

When selecting the *Benzocaine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Benzocaine	4	5	113

Second-stage model

For differentiation of the substance/substance group *Benzocaine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Benzocaine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Benzocaine	12341904	20843	40	1411055
Caelo	Benzocaine	13213509	21563	60	1706017
Fagron	Benzocaine	14G02-B01-306980	23569	40	20140723
Fagron	Benzocaine	16D13-B01-342411	23986	40	1807429

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Benzocaine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 190 spectra of 5 reference samples from the substance/substance group *Benzocaine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Benzocaine	161740	22641	40

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Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Benzocaine	172174	23628	40
Caelo	Benzocaine	182778	24378	40
Caelo	Benzocaine	190220	24531	40
Fagron	Benzocaine	12E04-N06	21083	30

- 118952 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 311 spectra from 194 *Apo-Ident* customers from 121 batches from the substance/substance group *Benzocaine*.
- Among them are spectra of independent samples from 114 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Benzocaine	KNC1643J15	1
AHD	Benzocaine	16174001	1
Anzag / Noweda	Benzocaine	1321351	1
Caelo	Benzocaine	11127508	1
Caelo	Benzocaine	11127506	1
Caelo	Benzocaine	12115007	5
Caelo	Benzocaine	91062169	1
Caelo	Benzocaine	19031301	1
Caelo	Benzocaine	12115011	3
Caelo	Benzocaine	10072603	3
Caelo	Benzocaine	5021401	1
Caelo	Benzocaine	13213502	5
Caelo	Benzocaine	3784947	1
Caelo	Benzocaine	13L06-B02	1
Caelo	Benzocaine	6031501	1
Caelo	Benzocaine	13213515	3
Caelo	Benzocaine	15227302	10
Caelo	Benzocaine	15227307	4
Caelo	Benzocaine	15227301	2
Caelo	Benzocaine	15227311	2
Caelo	Benzocaine	15227312	2
Caelo	Benzocaine	11031703	1
Caelo	Benzocaine	16030403	1
Caelo	Benzocaine	16174007	7
Caelo	Benzocaine	15227313	1
Caelo	Benzocaine	161740075429	1
Caelo	Benzocaine	16174008	1
Caelo	Benzocaine	161740195459	1
Caelo	Benzocaine	16174015	1
Caelo	Benzocaine	18041803	1
Caelo	Benzocaine	16174020	1
Caelo	Benzocaine	16174017	2
Caelo	Benzocaine	16D13-B01_348062	1
Caelo	Benzocaine	18018808	2

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Supplier	Substance	Batch	Spectra
Caelo	Benzocaine	18018806	1
Caelo	Benzocaine	18277802	4
Caelo	Benzocaine	18277806	1
Caelo	Benzocaine	18277805	1
Caelo	Benzocaine	19022001	1
Caelo	Benzocaine	19022004	2
Caelo	Benzocaine	16174014	11
Caelo	Benzocaine	15C19-B04-322019	1
Caelo	Benzocaine	16D13-B01-345969	1
Caelo	Benzocaine	16174005	1
Caelo	Benzocaine	13L06-B02-294112	2
Caelo	Benzocaine	12341906	1
Caelo	Benzocaine	1(19022001)	1
Caelo	Benzocaine	15227315	4
Caelo	Benzocaine	15227314	4
Caelo	Benzocaine	16D13-B01-348062	3
Caelo	Benzocaine	16174019	6
Caelo	Benzocaine	12115008	2
Caelo	Benzocaine	2412M-01118	1
Caelo	Benzocaine	1515I-01118	1
Caelo	Benzocaine	19022006	1
Caelo	Benzocaine	13213518	1
Caelo	Benzocaine	15227317	1
Caelo	Benzocaine	15c19-b04-325359	1
Caelo	Benzocaine	18018804	6
Caelo	Benzocaine	16174001	7
Caelo	Benzocaine	18277801	3
Caelo	Benzocaine	14277502	4
Caelo	Benzocaine	161740077	1
Caelo	Benzocaine	18018801	10
Caelo	Benzocaine	16D13-B01-334195	1
Caesar & Loretz GmbH	Benzocaine	18018808	1
Caesar & Loretz GmbH	Benzocaine	19022006	1
Caesar & Loretz GmbH	Benzocaine	19022004	1
Caesar & Loretz GmbH	Benzocaine	192710003	1
Caesar & Loretz GmbH / ...	Benzocaine	16174019	1
Euro OTC	Benzocaine	15227313	1
Euro OTC	Benzocaine	13L06-B02-297505	1
Euro OTC	Benzocaine	15227314	1
Fagron	Benzocaine	BZ-08/11-12	1
Fagron	Benzocaine	11/22-N3	1
Fagron	Benzocaine	11/22-N03	1
Fagron	Benzocaine	12341904	1
Fagron	Benzocaine	11k08-B40-291841	1
Fagron	Benzocaine	11k08-b40-291841	1
Fagron	Benzocaine	13L06-B02-294112	4
Fagron	Benzocaine	400313	1
Fagron	Benzocaine	14G02-B01-310324	8
Fagron	Benzocaine	15227307	1
Fagron	Benzocaine	15C19-B04-316239	2
Fagron	Benzocaine	15C19-B04	1
Fagron	Benzocaine	14G02-B01-318318	2
Fagron	Benzocaine	15C19-B04-322019	5
Fagron	Benzocaine	15C-19-B04-325359	1
Fagron	Benzocaine	13F06N10	1
Fagron	Benzocaine	15C19-B04-325359	3
Fagron	Benzocaine	16D13	1
Fagron	Benzocaine	16D13B01341861	2
Fagron	Benzocaine	18F18-B50-352171	3
Fagron	Benzocaine	16D113-B01-345969	1

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Supplier	Substance	Batch	Spectra
Fagron	Benzocaine	18F18-B50-352167	2
Fagron	Benzocaine	581015	1
Fagron	Benzocaine	C0011803001	1
Fagron	Benzocaine	18F18-B50	2
Fagron	Benzocaine	13L06-B02-300494	1
Fagron	Benzocaine	18F29-B07-190519	6
Fagron	Benzocaine	13F06-N10	1
Fagron	Benzocaine	14G02B01318318	1
Fagron	Benzocaine	11K08-B40-291841	5
Fagron	Benzocaine	18F18-B50-353577	2
Fagron	Benzocaine	BZ-27/1112	1
Fagron	Benzocaine	104210-0001	1
Fagron	Benzocaine	16D13-B01-348062	1
Fagron	Benzocaine	10K02-N01	1
Fagron	Benzocaine	12E04-N06	9
Fagron	Benzocaine	4413E-01118	1
Fagron	Benzocaine	13L06-B02	4
Fagron	Benzocaine	18F29B07190519	1
Fagron	Benzocaine	13L06-B02-300494	5
Fagron	Benzocaine	12E014-N06	1
Fagron	Benzocaine	13L06Bo2	1
Fagron	Benzocaine	16D13-B01-345969	1
Fagron	Benzocaine	11K08-B40-291840	1
Fagron	Benzocaine	15C19-B04-308254	1
Fagron	Benzocaine	12H10-N06	3
Fagron	Benzocaine	13L06-B02_297505	1
Fagron	Benzocaine	16D13-B01-330168	1
Fagron	Benzocaine	16D13-B01-337264	1
Fagron	Benzocaine	16D13-B01	1
Fagron	Benzocaine	16D13-B01-334195	1
Fagron	Benzocaine	11K08-B40	4
Fagron	Benzocaine	13L06-B02-294100	2
Fagron	Benzocaine	18J31-B02-193431	1
Fargon	Benzocaine	12H10-N06	1
Fargon/Sana	Benzocaine	11K08-290049	1
Fargron	Benzocaine	13L06-B02-294112	1
Fiebig	Benzocaine	13L06-B02-300494	1
Fiebig	Benzocaine	15C19-B04-325359	1
Fiebig	Benzocaine	18018801	1
Gehe	Benzocaine	111214	1
Gehe	Benzocaine	15C19-B04	1
Gehe	Benzocaine	16D13-B01-337264	1
Gehe	Benzocaine	18J31-B02-193431	1
Kehr	Benzocaine	16D13-B01-330168	1
Kehr	Benzocaine	15C19-B04-325359	1
L12	Benzocaine	16D13-B01-348062	1
Caelo	Benzocaine	13213516	1
Phoenix	Benzocaine	12H10-N06	1
Phoenix	Benzocaine	19022001	2
Phoenix	Benzocaine	19022006	1
Phönix	Benzocaine	13F06-N10	1
Sanacorp	Benzocaine	13213502	1
Sanacorp	Benzocaine	13213506	1
Sanacorp W.E:07.01.14 ...	Benzocaine	13213502	1
Caelo	Benzocaine	13213509	6
Caelo	Benzocaine	12341904	6
Caelo	Benzocaine		1
Fagron	Benzocaine	16D13-B01-342411	3
s.Prüfprotokoll	Benzocaine		1

- 110 936 spectra from 742 *Apo-Ident* customers from a total of 31 772 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Benzocaine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Benzocaine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	170	20	118 952
Type C	0	283	28	110 936

The substance/substance group *Benzocaine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	89.4737 % (> 87.8947 %)
Type C	100.0000 % (> 99.8899 %)	90.9968 % (> 90.0322 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Benzocaine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bismuth gallath, basic	65.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Benzocaine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23986	23986	0.00	76.43
20843	20843	0.00	75.73
21563	21563	0.00	76.10
23569	23986	3.51	75.98

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Benzoic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20041-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Benzoic acid; Acidum benzoicum

Special notes

When selecting the *Benzoic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Benzoic acid	3	2	20

Second-stage model

For differentiation of the substance/substance group *Benzoic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Benzoic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Benzoic acid	13391310	21458	60	20131216
Caelo	Benzoic acid	15084614	22664	40	20150318
Caelo	Benzoic acid	15084611	23095	40	20150318
Caelo	Benzoic acid	15084614	23096	40	1707644
Caelo	Benzoic acid	15084614	23726	40	20150318

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Benzoic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 469 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Benzoic acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Benzoic acid	162701	24027	40
Caelo	Benzoic acid	190752	24532	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 45 spectra from 31 *Apo-Ident* customers from 22 batches from the substance/substance group *Benzoic acid*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Benzoic acid	KNC0558J15	1
ACM	Benzoic acid	KNC0396J17	1
Caelo	Benzoic acid	17327009	1
Anza	Benzoic acid	16001702	1
Anzag	Benzoic acid	16001708	1
Caelo	Benzoic acid	10156104	1
Caelo	Benzoic acid	13074605	3
Caelo	Benzoic acid	13391314	1
Caelo	Benzoic acid	15084603	3
Caelo	Benzoic acid	15084607	3
Caelo	Benzoic acid	1732701	1
Caelo	Benzoic acid	17327101	8
Caelo	Benzoic acid	15084701	1
Caelo	Benzoic acid	13074610	4
Caelo	Benzoic acid	17327006	1
Caelo	Benzoic acid	1339120	1
Caleo/Phoenix	Benzoic acid	15084607	1
Cealo	Benzoic acid	13391314	1
Fresenius	Benzoic acid	80715102	1
Gatt-Koller / Phoenix	Benzoic acid	2992/07131314	2
Caelo	Benzoic acid	13391320	1
Caelo	Benzoic acid	16001714	3
Phönix	Benzoic acid	13074605	2
Caelo	Benzoic acid	13391310	1
Caelo	Benzoic acid	15084614	1

- 111 202 spectra from 742 *Apo-Ident* customers from a total of 31 869 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Benzoic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Benzoic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	41	4	111 202

The substance/substance group *Benzoic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	91.1111 % (> 84.4444 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Benzoic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Acetylsalicylic acid	51.89	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Benzoic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21458	23096	11.94	40.96
22664	23096	13.30	41.23
23095	23096	10.73	41.47
23096	23096	0.00	44.62
23726	23096	4.21	43.34

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Benzydamine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20624-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Benzydamine hydrochloride; Benzydamini hydrochloridum

Special notes

When selecting the *Benzydamine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Benzydamine hydrochloride	3	3	36

Second-stage model

For differentiation of the substance/substance group *Benzydamine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Benzydamine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Benzydamine hydr...	AP300111801004B	24411	40	20180418
Fagron	Benzydamine hydr...	14I30-B04-300713	21699	45	AR-15-FG-015977-01
Fagron	Benzydamine hydr...	15I17-B02-315060	22268	60	20151211

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 145 spectra of 3 reference samples from the substance/substance group *Benzydamine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 544 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Benzydamine hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Benzydamine hydrochloride	16D05-B50-332333	23203	40
Fagron	Benzydamine hydrochloride	17H01-B03-345050	23942	40
Fagron	Benzydamine hydrochloride	18H29-B02-355663	24445	40

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Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Benzydamine hydrochloride	16D05-B50-332333	23204	40

- 118 982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 56 spectra from 50 *Apo-Ident* customers from 39 batches from the substance/substance group *Benzydamine hydrochloride*.
- Among them are spectra of independent samples from 35 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag/ Audov	Benzydamine hydrochloride	AP300111801004B	1
Audor Pharma	Benzydamine hydrochloride	300111702007b	1
Audor Pharma	Benzydamine hydrochloride	AP300111702007B	3
Audor Pharma	Benzydamine hydrochloride	300111702007B	1
Caelo	Benzydamine hydrochloride	17H01-B03-345050	2
Fagron	Benzydamine hydrochloride	13H19_N06	1
Fagron	Benzydamine hydrochloride	13A15-N03	1
Fagron	Benzydamine hydrochloride	14B25-B01-294054	1
Fagron	Benzydamine hydrochloride	1503309P	1
Fagron	Benzydamine hydrochloride	15I17-B02	1
Fagron	Benzydamine hydrochloride	1503313P	1
Fagron	Benzydamine hydrochloride	25021710	1
Fagron	Benzydamine hydrochloride	12J10-N03	1
Fagron	Benzydamine hydrochloride	16D05-b50-332334	1
Fagron	Benzydamine hydrochloride	16D05-B50-332333	1
Fagron	Benzydamine hydrochloride	16d05-b50-332333	1
Fagron	Benzydamine hydrochloride	16D05-B50-332334	1
Fagron	Benzydamine hydrochloride	1703305P	1
Fagron	Benzydamine hydrochloride	17H01-B03_34641	1
Fagron	Benzydamine hydrochloride	17H01-B03-348469	2
Fagron	Benzydamine hydrochloride	18H29-B02-354330	1
Fagron	Benzydamine hydrochloride	18H29-B02-358710	2
Fagron	Benzydamine hydrochloride	17H01-B03-345051	2
Fagron	Benzydamine hydrochloride	17H01-B03-345050	4
Fagron	Benzydamine hydrochloride	18H29-B02-354329	3
Fagron	Benzydamine hydrochloride	16B09-B05-320007	1
Fagron	Benzydamine hydrochloride	18H29-B02-355663	1
Fagron	Benzydamine hydrochloride	18H29-B02-361603	1
Fagron	Benzydamine hydrochloride	13H19-N06	1
Fagron	Benzydamine hydrochloride	12K07-N16	1
Fagron	Benzydamine hydrochloride	15A14-B05	1
Fagron	Benzydamine hydrochloride	16B09-B05-318272	2
Fagron	Benzydamine hydrochloride	3280417	1
Fagron	Benzydamine hydrochloride	15A14-B05-303068	1
Fagron	Benzydamine hydrochloride	1503315P	1
Fagron	Benzydamine hydrochloride	12C20-N02	1
Fresenius	Benzydamine hydrochloride	30062015099	1

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Supplier	Substance	Batch	Spectra
Gehe	Benzydamine hydrochloride	AP300111801004B	1
Caelo	Benzydamine hydrochloride	18H29B02-358710	1
Caelo	Benzydamine hydrochloride	12K07-N16	1
SANACORP	Benzydamine hydrochloride	18H29-B02	1
Audor Pharma	Benzydamine hydrochloride	AP300111801004B	2
Fagron	Benzydamine hydrochloride		1

- 111 191 spectra from 742 *Apo-Ident* customers from a total of 31 852 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Benzydamine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Benzydamine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	145	0	110 544
Type B	0	160	0	118 982
Type C	0	56	0	111 191

The substance/substance group *Benzydamine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.8621 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 89.2857 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Benzydamine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Doxylamine hydrogen succinate	31.24	—
Diltiazem hydrochloride	34.59	—
Cocaine hydrochloride	43.24	—
Diphenhydramine hydrochloride	48.92	—
Ethyl hydrogen fumarate calcium	50.74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Benzylamine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21699	21699	0.00	28.03
22268	21699	2.94	27.43
24411	21699	8.28	30.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Betaine monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20498-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betaine monohydrate; Betainum monohydricum

Special notes

When selecting the *Betaine monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Betaine monohydrate	3	1	3

Second-stage model

For differentiation of the substance/substance group *Betaine monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Betaine monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Betaine monohydr. . .	12336602	20991	40	1403327
Fagron	Betaine monohydr. . .	14I26-B06-309878	21956	60	20141212
Fagron	Betaine monohydr. . .	18H13-B01-355585	24585	40	20180907

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Betaine monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Betaine monohydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Betaine monohydrate	16H03-B04-330370	23092	40
Fagron	Betaine monohydrate	16H03-B04-330370	23378	40

- 119 062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Betaine monohydrate*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Betaine monohydrate	14A14-B02-292983	1
Caelo	Betaine monohydrate	4312172831	1
Fagron	Betaine monohydrate	16H03-B04-330370	1

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Betaine monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Betaine monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	3	0	111 244

The substance/substance group *Betaine monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Betaine monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	50.31	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Betaine monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20991	20991	0.00	84.85
21956	20991	4.14	84.86
24585	20991	3.83	84.83

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Betamethasone dipropionate, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20930-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betamethasone dipropionate, micronized; Betamethasoni dipropionas micronisatum

Special notes

When selecting the *Betamethasone dipropionate, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Betamethasone dipropionate, micronized	6	7	164

Second-stage model

For differentiation of the substance/substance group *Betamethasone dipropionate, micronized* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Betamethasone dipropionate, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Betamethasone di...	13372501	21250	40	AR-15-FG-005428-01
Caelo	Betamethasone di...	13372501	21250SI	45	AR-15-FG-005428-01
Caelo	Betamethasone di...	13236803	21366	50	20130730
Caelo	Betamethasone di...	13236803	21366SI	46	20130730
Caelo	Betamethasone di...	13236803	21367	40	20130730
Euro OTC	Betamethasone di...	1311023-01	21716	60	1505455
Euro OTC	Betamethasone di...	1311023-01	21716SI	46	1505455
Euro OTC	Betamethasone di...	1601034	22372	45	20160204*
Euro OTC	Betamethasone di...	1601034	22372SI	45	20160204*
Fagron	Betamethasone di...	13I17-N05	20930	40	1401377
Fagron	Betamethasone di...	13I17-N05	20952	80	20130926
Fagron	Betamethasone di...	16C04-B03-324513	22898	40	20160421
Fagron	Betamethasone di...	16C04-B03-324513	22898SI	39	20160421

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 616 spectra of 13 reference samples from the substance/substance group *Betamethasone dipropionate, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 073 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 551 spectra of 15 reference samples from the substance/substance group *Betamethasone dipropionate, micronized*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Betamethasone dipropionate, ...	171059	23342	40
Caelo	Betamethasone dipropionate, ...	173536	23839	40
Euro OTC	Betamethasone dipropionate, ...	1610014	22851	40
Euro OTC	Betamethasone dipropionate, ...	1705020	23539	40
Euro OTC	Betamethasone dipropionate, ...	1801045	24090	40
Euro OTC	Betamethasone dipropionate, ...	1811007	24343	40
Euro OTC	Betamethasone dipropionate, ...	1907034	24796	40
Caelo	Betamethasone dipropionate, ...	13236803	21367SI [†]	60
Caelo	Betamethasone dipropionate, ...	171059	23342SI	20
Caelo	Betamethasone dipropionate, ...	173536	23839SI	25
Euro OTC	Betamethasone dipropionate, ...	1610014	22851SI	30
Euro OTC	Betamethasone dipropionate, ...	1705020	23539SI	27
Euro OTC	Betamethasone dipropionate, ...	1801045	24090SI	39
Euro OTC	Betamethasone dipropionate, ...	1811007	24343SI	30
Euro OTC	Betamethasone dipropionate, ...	1907034	24796SI	40

- 118 591 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 683 spectra from 285 *Apo-Ident* customers from 177 batches from the substance/substance group *Betamethasone dipropionate, micronized*.
- Among them are spectra of independent samples from 164 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Betamethasone dipropionate, ...	18B06-B05-346219	1
Caelo	Betamethasone dipropionate, ...	15412906	11
Alliance Health 24.01.2...	Betamethasone dipropionate, ...	13/17-N05	1
Fagron	Betamethasone dipropionate, ...	18B06B05352731	2
Anzag	Betamethasone dipropionate, ...	12114513	2
Bombastus	Betamethasone dipropionate, ...	12B27N08	1
cae	Betamethasone dipropionate, ...	17353601	1
Caelo	Betamethasone dipropionate, ...	13125701	3

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Betamethasone dipropionate, ...	13372504	5
Caelo	Betamethasone dipropionate, ...	12114507	2
Caelo	Betamethasone dipropionate, ...	12114506	1
Caelo	Betamethasone dipropionate, ...	12114512	1
Caelo	Betamethasone dipropionate, ...	1210020-01	1
Caelo	Betamethasone dipropionate, ...	13023002	5
Caelo	Betamethasone dipropionate, ...	1325702	1
Caelo	Betamethasone dipropionate, ...	13125703	5
Caelo	Betamethasone dipropionate, ...	13236801	6
Caelo	Betamethasone dipropionate, ...	13236802	4
Caelo	Betamethasone dipropionate, ...	13236805	4
Caelo	Betamethasone dipropionate, ...	18121306	1
Caelo	Betamethasone dipropionate, ...	12114513	1
Caelo	Betamethasone dipropionate, ...	13236806	3
Caelo	Betamethasone dipropionate, ...	13372503	7
Caelo	Betamethasone dipropionate, ...	13372516	4
Caelo	Betamethasone dipropionate, ...	15163301	14
Caelo	Betamethasone dipropionate, ...	15163302	6
Caelo	Betamethasone dipropionate, ...	15163303	10
Caelo	Betamethasone dipropionate, ...	13372512	1
Caelo	Betamethasone dipropionate, ...	1503003-02	1
Caelo	Betamethasone dipropionate, ...	15163204	1
Caelo	Betamethasone dipropionate, ...	15163305	1
Caelo	Betamethasone dipropionate, ...	15412901	1
Caelo	Betamethasone dipropionate, ...	15238701	25
Caelo	Betamethasone dipropionate, ...	150605BD	1
Caelo	Betamethasone dipropionate, ...	15412905	1
Caelo	Betamethasone dipropionate, ...	15H28-B06	1
Caelo	Betamethasone dipropionate, ...	15412909	1
Caelo	Betamethasone dipropionate, ...	15412916	1
Caelo	Betamethasone dipropionate, ...	3170717	1
Caelo	Betamethasone dipropionate, ...	15412914	7
Caelo	Betamethasone dipropionate, ...	15H28-B06-313088	1
Caelo	Betamethasone dipropionate, ...	17105903	1
Caelo	Betamethasone dipropionate, ...	17105901	13
Caelo	Betamethasone dipropionate, ...	17105902	12
Caelo	Betamethasone dipropionate, ...	17B16-B04-332220	1
Caelo	Betamethasone dipropionate, ...	18041819	1
Caelo	Betamethasone dipropionate, ...	13023002NP	1
Caelo	Betamethasone dipropionate, ...	17105911	4
Caelo	Betamethasone dipropionate, ...	1735601	1
Caelo	Betamethasone dipropionate, ...	1801045-01	3
Caelo	Betamethasone dipropionate, ...	17353603	9
Caelo	Betamethasone dipropionate, ...	18090603	9
Caelo	Betamethasone dipropionate, ...	18090602	2
Caelo	Betamethasone dipropionate, ...	18090607	6
Caelo	Betamethasone dipropionate, ...	18293406	4
Caelo	Betamethasone dipropionate, ...	18293408	3
Caelo	Betamethasone dipropionate, ...	17105909	2
Caelo	Betamethasone dipropionate, ...	18090608	4
Caelo	Betamethasone dipropionate, ...	1811007-01	1
Caelo	Betamethasone dipropionate, ...	18B06-B05-350473	1
Caelo	Betamethasone dipropionate, ...	18292406	1
Caelo	Betamethasone dipropionate, ...	13023001	3
Caelo	Betamethasone dipropionate, ...	15H28B06313088	1
Caelo	Betamethasone dipropionate, ...	15412907	5
Caelo	Betamethasone dipropionate, ...	17105905	4
Caelo	Betamethasone dipropionate, ...	17B16-B04	1
Caelo	Betamethasone dipropionate, ...	13023005	7
Caelo	Betamethasone dipropionate, ...	14C03-B06-296837	1

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Supplier	Substance	Batch	Spectra
Caelo	Betamethasone dipropionate, ...	15412910	6
Caelo	Betamethasone dipropionate, ...	12114501	1
Caelo	Betamethasone dipropionate, ...	140507	1
Caelo	Betamethasone dipropionate, ...	18090606	9
Caelo	Betamethasone dipropionate, ...	17353601	15
Caelo	Betamethasone dipropionate, ...	17105907	4
Caelo	Betamethasone dipropionate, ...	13372514	10
Caelo	Betamethasone dipropionate, ...	15412903	2
Caelo	Betamethasone dipropionate, ...	18293404	2
Caelo	Betamethasone dipropionate, ...	13372520	1
Caelo	Betamethasone dipropionate, ...	18B06-B05-352731	1
Caelo	Betamethasone dipropionate, ...	18293402	5
Caelo	Betamethasone dipropionate, ...	1303006-01	1
Caelo	Betamethasone dipropionate, ...	13372515	3
Caelo	Betamethasone dipropionate, ...	8K03-N13	1
Caelo	Betamethasone dipropionate, ...	13/17-N05	2
Caelo	Betamethasone dipropionate, ...	2109DM0B00111322	1
Caelo	Betamethasone dipropionate, ...	15412913	1
Caelo	Betamethasone dipropionate, ...	1705020-01	1
Caelo	Betamethasone dipropionate, ...	17015905	1
Caelo	Betamethasone dipropionate, ...	18090601	4
Caelo	Betamethasone dipropionate, ...	13236801ok	1
Caelo	Betamethasone dipropionate, ...	1503003-01	2
Caelo	Betamethasone dipropionate, ...	15163304	9
Caesar & Loretz GmbH	Betamethasone dipropionate, ...	17105902	1
Caesar & Loretz GmbH	Betamethasone dipropionate, ...	18293402	1
Caesar & Loretz GmbH	Betamethasone dipropionate, ...	18293404	1
Caesar & Loretz GmbH	Betamethasone dipropionate, ...	18293406	2
Caesar & Loretz GmbH	Betamethasone dipropionate, ...	18293408	1
Caesar & Loretz GmbH / ...	Betamethasone dipropionate, ...	18293406	1
Caesar & Loretz GmbH, A...	Betamethasone dipropionate, ...	18090603	1
Cealo	Betamethasone dipropionate, ...	17353601	1
Cealo/Sanacorp	Betamethasone dipropionate, ...	13125701	1
Delta	Betamethasone dipropionate, ...	18B06-B05-346219	1
euro AHD	Betamethasone dipropionate, ...	1801045-015715	1
euro AHD	Betamethasone dipropionate, ...	1801045-015787	1
Euro OTC	Betamethasone dipropionate, ...	121002001	1
Euro OTC	Betamethasone dipropionate, ...	1303006-01	2
Euro OTC	Betamethasone dipropionate, ...	1305041-02	3
Euro OTC	Betamethasone dipropionate, ...	131102301	2
Euro OTC	Betamethasone dipropionate, ...	1610014-01	27
Euro OTC	Betamethasone dipropionate, ...	1610014-015308	1
Euro OTC	Betamethasone dipropionate, ...	19070324-01	1
Euro OTC	Betamethasone dipropionate, ...	1303006-02	1
Euro OTC	Betamethasone dipropionate, ...	1503003-02	8
Euro OTC	Betamethasone dipropionate, ...	1303006/01	1
Euro OTC	Betamethasone dipropionate, ...	150300302	1
Euro OTC	Betamethasone dipropionate, ...	15163304	1
Euro OTC	Betamethasone dipropionate, ...	1907034-01	1
Euro OTC	Betamethasone dipropionate, ...	1311023-02	5
Euro OTC	Betamethasone dipropionate, ...	170502001	1
Euro OTC	Betamethasone dipropionate, ...	180808185	1
Euro OTC	Betamethasone dipropionate, ...	180104501	2
Euro OTC	Betamethasone dipropionate, ...	130541-01	1
Euro OTC	Betamethasone dipropionate, ...	12114511	2
Euro OTC	Betamethasone dipropionate, ...	1305041-01	10
Euro OTC	Betamethasone dipropionate, ...	13125702	1
Euro OTC	Betamethasone dipropionate, ...	13372501	1
Euro OTC	Betamethasone dipropionate, ...	1503003-01	10
euro//Noweda	Betamethasone dipropionate, ...	1705030-01	1

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Supplier	Substance	Batch	Spectra
EUro/AHD	Betamethasone dipropionate, ...	1303006-01	3
Euro/Gehe	Betamethasone dipropionate, ...	1601034-01	1
Euro/Sanacorp	Betamethasone dipropionate, ...	1503003-02	1
Euro OTC	Betamethasone dipropionate, ...	1801045-01	13
Euro OTC	Betamethasone dipropionate, ...	1601034-01	20
Euro OTC	Betamethasone dipropionate, ...	1506016-02	1
Euro OTC	Betamethasone dipropionate, ...	160103401	1
Fagron	Betamethasone dipropionate, ...	14C03-B06	2
Fagron	Betamethasone dipropionate, ...	12827-N08	1
Fagron	Betamethasone dipropionate, ...	10E19-N03	1
Fagron	Betamethasone dipropionate, ...	11D26-N06	2
Fagron	Betamethasone dipropionate, ...	12C21-N13	1
Fagron	Betamethasone dipropionate, ...	13023004	1
Fagron	Betamethasone dipropionate, ...	13/17-N05	13
Fagron	Betamethasone dipropionate, ...	13/17-n05	1
Fagron	Betamethasone dipropionate, ...	13J16-B01-291845	2
Fagron	Betamethasone dipropionate, ...	13j16-b01-291845	1
Fagron	Betamethasone dipropionate, ...	13i17-N05	1
Fagron	Betamethasone dipropionate, ...	15H28-B06-313088	4
Fagron	Betamethasone dipropionate, ...	14C03-B03-296838	1
Fagron	Betamethasone dipropionate, ...	16C04-B03-320851	1
Fagron	Betamethasone dipropionate, ...	16C04-B03-320852	1
Fagron	Betamethasone dipropionate, ...	2109DM0B0011322	1
Fagron	Betamethasone dipropionate, ...	19041706	1
Fagron	Betamethasone dipropionate, ...	17B16-B04-332224	4
Fagron	Betamethasone dipropionate, ...	18B06-B05-346218	3
Fagron	Betamethasone dipropionate, ...	18B06-B05-347338	2
Fagron	Betamethasone dipropionate, ...	18Bo6-B0o5-352731	1
Fagron	Betamethasone dipropionate, ...	18B06-B05-352731	1
Fagron	Betamethasone dipropionate, ...	18/27-B03-357221	1
Fagron	Betamethasone dipropionate, ...	17b16b04332218	1
Fagron	Betamethasone dipropionate, ...	18b06-b05-350473	1
Fagron	Betamethasone dipropionate, ...	17E22-B06-336993	3
Fagron	Betamethasone dipropionate, ...	14C03-B06-296837	6
Fagron	Betamethasone dipropionate, ...	9J05-N09	1
Fagron	Betamethasone dipropionate, ...	11K28-N10	2
Fagron	Betamethasone dipropionate, ...	17E22B06336993	1
Fagron	Betamethasone dipropionate, ...	20171127Ma5	1
Fagron	Betamethasone dipropionate, ...	17816B04332224	1
Fagron	Betamethasone dipropionate, ...	17B16-B04-332219-201	1
Fagron	Betamethasone dipropionate, ...	12B27-N08	6
Fagron	Betamethasone dipropionate, ...	16C04-B03-320850	2
Fagron	Betamethasone dipropionate, ...	17B16-B04	1
Fagron	Betamethasone dipropionate, ...	BDP101/0417	1
Fagron	Betamethasone dipropionate, ...	17E22-B06-336705	1
Fagron	Betamethasone dipropionate, ...	17B6-B04-332217	1
Fagron	Betamethasone dipropionate, ...	18B06-B05-354808	2
Fagron	Betamethasone dipropionate, ...	18B06B05347338	1
Fagron	Betamethasone dipropionate, ...	18B06B05354807	1
Fagron	Betamethasone dipropionate, ...	18B06-B05-354807	4
Fagron	Betamethasone dipropionate, ...	13j16-B01-291844	1
Fagron	Betamethasone dipropionate, ...	17B16-B04-332217	6
Fagron	Betamethasone dipropionate, ...	18B06-B05-350473	5
Fagron	Betamethasone dipropionate, ...	8K03-N13	1
Fagron	Betamethasone dipropionate, ...	17H16-B04-340537	1
Fagron	Betamethasone dipropionate, ...	1317-N05	1
Fagron	Betamethasone dipropionate, ...	15H25-B06-313088	1
Fagron	Betamethasone dipropionate, ...	1601034-01	1
Fagron	Betamethasone dipropionate, ...	18B06-B05	5
Fagron	Betamethasone dipropionate, ...	18I127-B03-357222	1

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Supplier	Substance	Batch	Spectra
Fagron	Betamethasone dipropionate, ...	18B06-B05-346219	1
Fargon	Betamethasone dipropionate, ...	16C04-B033-24513	1
Fargon/ Noweda	Betamethasone dipropionate, ...	13/17-N05	1
Fargon/AllianceH.	Betamethasone dipropionate, ...	17H16B04-340537	1
Fragon	Betamethasone dipropionate, ...	18B06-B05-352731	1
Gehe	Betamethasone dipropionate, ...	15238701	1
Gehe	Betamethasone dipropionate, ...	1705020-01	1
GEHE	Betamethasone dipropionate, ...	15412914	1
Hirsch	Betamethasone dipropionate, ...	1303006-01	1
Kehr	Betamethasone dipropionate, ...	1705020-01	1
Fagron	Betamethasone dipropionate, ...	17E22-B06-335244	3
Fagron	Betamethasone dipropionate, ...	18B06B0534996	1
Klosterring	Betamethasone dipropionate, ...	17B16-B04-332219	2
Noweda	Betamethasone dipropionate, ...	13236802	1
Noweda	Betamethasone dipropionate, ...	13236803	1
Noweda	Betamethasone dipropionate, ...	BDP014/1115	1
Euro OTC	Betamethasone dipropionate, ...	17B16-B04-332218	1
Fagron	Betamethasone dipropionate, ...	BDP102/0817	1
Euro OTC	Betamethasone dipropionate, ...	1705020-01	15
Phoenix	Betamethasone dipropionate, ...	13236806	1
Phoenix	Betamethasone dipropionate, ...	1610014-01	1
Phoenix	Betamethasone dipropionate, ...	1705020-01	1
Phoenix	Betamethasone dipropionate, ...	1811007-01	1
Phoenix 03.04.20147	Betamethasone dipropionate, ...	13236805	1
phönix	Betamethasone dipropionate, ...	15163304	1
PHÖNIX	Betamethasone dipropionate, ...	17353603	1
Caelo	Betamethasone dipropionate, ...	17105906	10
Sanacorp	Betamethasone dipropionate, ...	1610014-01	1
Sanacorp	Betamethasone dipropionate, ...	1705020-01	1
Sanacorp	Betamethasone dipropionate, ...	17B16-B04-332217	2
Sanacorp	Betamethasone dipropionate, ...	170502001	1
Sanacorp	Betamethasone dipropionate, ...	17105911	1
Sanacorp	Betamethasone dipropionate, ...	18B06-B05-346218	1
Sanacorp	Betamethasone dipropionate, ...	BDP102/0817	1
Sanacorp	Betamethasone dipropionate, ...	18090607	1
SANACORP	Betamethasone dipropionate, ...	18293404	1
Sanacorp WE: 12.08.17 ...	Betamethasone dipropionate, ...	15238701	1
Caelo	Betamethasone dipropionate, ...	AKD11	1
Fagron	Betamethasone dipropionate, ...	1801045-01	1
WE:05.04.2016 Phönix	Betamethasone dipropionate, ...	15163304	4
WE:09.12.2016	Betamethasone dipropionate, ...	15163301	1
Caelo	Betamethasone dipropionate, ...	13372501	3
Caelo	Betamethasone dipropionate, ...	13236803	1
Euro OTC	Betamethasone dipropionate, ...	1311023-01	10
Fagron	Betamethasone dipropionate, ...	13I17-N05	12
Fagron	Betamethasone dipropionate, ...		4
	Betamethasone dipropionate, ...	13/17-N05	2
Caelo	Betamethasone dipropionate, ...		1
	Betamethasone dipropionate, ...		1

- 110 564 spectra from 742 *Apo-Ident* customers from a total of 31 717 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Betamethasone dipropionate, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Betamethasone dipropionate, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	616	0	110 073
Type B	0	551	0	118 591
Type C	0	666	17	110 564

The substance/substance group *Betamethasone dipropionate, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0260 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.9111 %)
Type C	100.0000 % (> 99.8899 %)	97.5110 % (> 97.0717 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Betamethasone dipropionate, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clobetasol propionate	9.54	59.26
Beclometasone dipropionate	19.95	33.82
Dexamethasone acetate	24.19	—
Prednisolone acetate	44.90	—
Dexamethasone	50.40	—
⋮	⋮	⋮
Oxybutynin hydrochloride	>50	91.99
Gentamicin sulfate	>50	238.23
Sodium citrate	>50	410.58
Sodium benzoate	>50	656.26

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Betamethasone dipropionate, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21367	21250	2.16	13.26
22898	20930	2.61	15.72
21716	21716	0.00	13.95
22372	22372	0.00	13.41
20930	20930	0.00	15.80
20952	20930	4.37	12.82
21366	21250	1.42	13.91
21250	21250	0.00	13.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Betamethasone valerate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20026-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betamethasone valerate; Betamethasoni valeras

Special notes

When selecting the *Betamethasone valerate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Betamethasone valerate	10	6	492

Second-stage model

For differentiation of the substance/substance group *Betamethasone valerate* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Betamethasone valerate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Betamethasone va...	13091213	21215	40	20130506
Caelo	Betamethasone va...	13225507	21588	54	1706018
Euro OTC	Betamethasone va...	1208014-01	20920	40	20120928
Euro OTC	Betamethasone va...	1406019-01	21645	60	20140725
Euro OTC	Betamethasone va...	1510037	22249	60	20151215*
Euro OTC	Betamethasone va...	1510037	22249SI	30	20151215*
Euro OTC	Betamethasone va...	1610010	22861	40	20161116*
Euro OTC	Betamethasone va...	1811008	24349	40	20181207*
Euro OTC	Betamethasone va...	1811008	24349SI	30	20181207*
Fagron	Betamethasone va...	12K07-N23	20887	40	20121119
Fagron	Betamethasone va...	13K29-B32-288243	21566	60	20131210
Fagron	Betamethasone va...	13K05-B08-292651	21674	60	1511154

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 554 spectra of 12 reference samples from the substance/substance group *Betamethasone valerate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 135 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 459 spectra of 14 reference samples from the substance/substance group *Betamethasone valerate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Betamethasone valerate	170787	23332	40
Caelo	Betamethasone valerate	172716	23683	40
Euro OTC	Betamethasone valerate	1606023	22716	40
Euro OTC	Betamethasone valerate	1704019	23396	40
Euro OTC	Betamethasone valerate	1801024	23967	40
Euro OTC	Betamethasone valerate	1911001	24982	40
Caelo	Betamethasone valerate	13225507	21588 [†]	6
Caelo	Betamethasone valerate	170787	23332SI	20
Caelo	Betamethasone valerate	172716	23683SI	20
Euro OTC	Betamethasone valerate	1606023	22716SI	34
Euro OTC	Betamethasone valerate	1610010	22861SI [†]	30
Euro OTC	Betamethasone valerate	1704019	23396SI	29
Euro OTC	Betamethasone valerate	1801024	23967SI	40
Euro OTC	Betamethasone valerate	1911001	24982SI	40

- 118 683 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2552 spectra from 606 *Apo-Ident* customers from 523 batches from the substance/substance group *Betamethasone valerate*.
- Among them are spectra of independent samples from 491 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
/Sanacorp	Betamethasone valerate	17078701	1
A.H.D.	Betamethasone valerate	13D03-N07	1
agron/Krieger	Betamethasone valerate	12B2B-N01	1
AHC 01.07.13 EK 48,05	Betamethasone valerate	12K07-N23	1
AHD	Betamethasone valerate	1406019-02	2
AHD	Betamethasone valerate	15262607	1
AHD	Betamethasone valerate	15398515	1
AHD	Betamethasone valerate	17078714	1
AHD	Betamethasone valerate	18199902	1
Caelo	Betamethasone valerate	13G19-N01	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
AHD 15.06.16 EK:18,44	Betamethasone valerate	15398505	1
AHD 17.11.14 EK 18,11	Betamethasone valerate	13091205	1
Caelo	Betamethasone valerate	1610010-01	5
AHD/Fargon	Betamethasone valerate	14H28-Bo1-302865	1
AHDE / Cael 17.02.2015	Betamethasone valerate	13225516	1
AHL	Betamethasone valerate	15398501	1
ALH	Betamethasone valerate	15398512	1
Euro OTC	Betamethasone valerate	16270505	1
Alliance Health 06.02.2...	Betamethasone valerate	13091207	1
Alliance healthcare	Betamethasone valerate	13D03-N07	1
Alliance Healthcare	Betamethasone valerate	1610010-01	1
Bombastus	Betamethasone valerate	12L11-N01	1
Allianz Healthcare 27.0...	Betamethasone valerate	15075802	1
Anzag	Betamethasone valerate	12L11-N01	1
Euro OTC	Betamethasone valerate	1739002	1
Bombastus	Betamethasone valerate	1510037-01	1
Bombastus	Betamethasone valerate	1704019-01	4
Cael Sanacorp 05.02.2016	Betamethasone valerate	14H28-B01-302864	1
Caelo/Sanacorp	Betamethasone valerate	15075803	1
Caelo	Betamethasone valerate	16270505	13
Caelo	Betamethasone valerate	1108045-03	4
Caelo	Betamethasone valerate	11131909	1
Caelo	Betamethasone valerate	11131914	1
Caelo	Betamethasone valerate	18121206	1
Caelo	Betamethasone valerate	11131914	1
Caelo	Betamethasone valerate	12003410	1
Caelo	Betamethasone valerate	12003407	1
Caelo	Betamethasone valerate	12003411	3
Caelo	Betamethasone valerate	12003404	1
Caelo	Betamethasone valerate	12229802	3
Caelo	Betamethasone valerate	12K07-N23	1
Caelo	Betamethasone valerate	1113	1
Caelo	Betamethasone valerate	10296701	1
Caelo	Betamethasone valerate	12229804	3
Caelo	Betamethasone valerate	12003409	1
Caelo	Betamethasone valerate	13091201	2
Caelo	Betamethasone valerate	13091204	4
Caelo	Betamethasone valerate	13091209	4
Caelo	Betamethasone valerate	210112	1
Caelo	Betamethasone valerate	1208014-03	1
Caelo	Betamethasone valerate	B03041205	1
Caelo	Betamethasone valerate	14031407	1
Caelo	Betamethasone valerate	13225503	9
Caelo	Betamethasone valerate	18071403	1
Caelo	Betamethasone valerate	13225504	9
Caelo	Betamethasone valerate	13225508	9
Caelo	Betamethasone valerate	10296707	1
Caelo	Betamethasone valerate	14188603	5
Caelo	Betamethasone valerate	13225516	10
Caelo	Betamethasone valerate	13225607	1
Caelo	Betamethasone valerate	13012015C	1
Caelo	Betamethasone valerate	14C19-B02-292653	1
Caelo	Betamethasone valerate	14188608	6
Caelo	Betamethasone valerate	13K05_B08_292652	1
Caelo	Betamethasone valerate	14188609	5
Caelo	Betamethasone valerate	15075802	20
Caelo	Betamethasone valerate	14188610	6
Caelo	Betamethasone valerate	8081502	1
Caelo	Betamethasone valerate	15075805	6
Caelo	Betamethasone valerate	15075804	7

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Supplier	Substance	Batch	Spectra
Caelo	Betamethasone valerate	15075810	9
Caelo	Betamethasone valerate	1510037-01	2
Caelo	Betamethasone valerate	150758036	1
Caelo	Betamethasone valerate	123345	1
Caelo	Betamethasone valerate	15262609	3
Caelo	Betamethasone valerate	15262606	4
Caelo	Betamethasone valerate	15262613	1
Caelo	Betamethasone valerate	15398505	14
Caelo	Betamethasone valerate	1516-B07-319228	1
Caelo	Betamethasone valerate	160216BV	1
Caelo	Betamethasone valerate	15398515	23
Caelo	Betamethasone valerate	161125BV/15398512	1
Caelo	Betamethasone valerate	1606023-01	4
Caelo	Betamethasone valerate	15075811	1
Caelo	Betamethasone valerate	16270501	15
Caelo	Betamethasone valerate	15398512	17
Caelo	Betamethasone valerate	15398502	1
Caelo	Betamethasone valerate	15398503	2
Caelo	Betamethasone valerate	15L21-B03-318663	1
Caelo	Betamethasone valerate	15398504	3
Caelo	Betamethasone valerate	14188605	1
Caelo	Betamethasone valerate	15398514	3
Caelo	Betamethasone valerate	16270504	1
Caelo	Betamethasone valerate	16720513	1
Caelo	Betamethasone valerate	170401901	4
Caelo	Betamethasone valerate	17078103	1
Caelo	Betamethasone valerate	15/16-B07-317416	1
Caelo	Betamethasone valerate	17078705	1
Caelo	Betamethasone valerate	129711-5471	1
Caelo	Betamethasone valerate	311002517078712	1
Caelo	Betamethasone valerate	17G31B04338575	1
Caelo	Betamethasone valerate	17078719	15
Caelo	Betamethasone valerate	17078715	11
Caelo	Betamethasone valerate	17078716	1
Caelo	Betamethasone valerate	17271604	5
Caelo	Betamethasone valerate	1707815	2
Caelo	Betamethasone valerate	17271602	1
Caelo	Betamethasone valerate	17329003	9
Caelo	Betamethasone valerate	1801024-01	7
Caelo	Betamethasone valerate	17329017	6
Caelo	Betamethasone valerate	17329004	3
Caelo	Betamethasone valerate	17329011	3
Caelo	Betamethasone valerate	1729002	1
Caelo	Betamethasone valerate	18199907	15
Caelo	Betamethasone valerate	18199908	4
Caelo	Betamethasone valerate	18199933	5
Caelo	Betamethasone valerate	18199915	1
Caelo	Betamethasone valerate	10296705	2
Caelo	Betamethasone valerate	12229806	5
Caelo	Betamethasone valerate	17G31-B04-338575	1
Caelo	Betamethasone valerate	1488610	1
Caelo	Betamethasone valerate	14188604	8
Caelo	Betamethasone valerate	14G30-B05	1
Caelo	Betamethasone valerate	16B18-B02-322121	2
Caelo	Betamethasone valerate	17C29-B04-335676	1
Caelo	Betamethasone valerate	17C29-B04-334329	1
Caelo	Betamethasone valerate	18G03-B03-351731	1
Caelo	Betamethasone valerate	13091207	8
Caelo	Betamethasone valerate	18199902	16
Caelo	Betamethasone valerate	18199916	8

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Supplier	Substance	Batch	Spectra
Caelo	Betamethasone valerate	12229810	3
Caelo	Betamethasone valerate	15/16-B07-319228	2
Caelo	Betamethasone valerate	17329008	7
Caelo	Betamethasone valerate	17078707	1
Caelo	Betamethasone valerate	18199906	3
Caelo	Betamethasone valerate	12229808	12
Caelo	Betamethasone valerate	13091212	6
Caelo	Betamethasone valerate	12B28-N01	1
Caelo	Betamethasone valerate	13091206	1
Caelo	Betamethasone valerate	12229809	2
Caelo	Betamethasone valerate	31 (17329018)	1
Caelo	Betamethasone valerate	14188619	3
Caelo	Betamethasone valerate	1406019-02	2
Caelo	Betamethasone valerate	15398513	4
Caelo	Betamethasone valerate	1704019-01	11
Caelo	Betamethasone valerate	17329018	40
Caelo	Betamethasone valerate	13091205	11
Caelo	Betamethasone valerate	1526604	1
Caelo	Betamethasone valerate	16H22-B06-331273	1
Caelo	Betamethasone valerate	17271603	21
Caelo	Betamethasone valerate	17271601	4
Caelo	Betamethasone valerate	17329002	16
Caelo	Betamethasone valerate	18199932	10
Caelo	Betamethasone valerate	3303	1
Caelo	Betamethasone valerate	13225505	8
Caelo	Betamethasone valerate	15262602	4
Caelo	Betamethasone valerate	NT0597M	1
Caelo	Betamethasone valerate	15075809	3
Caelo	Betamethasone valerate	15398506	25
Caelo	Betamethasone valerate	15262612	1
Caelo	Betamethasone valerate	17K16-B08-347309	1
Caelo	Betamethasone valerate	18199903	2
Caelo	Betamethasone valerate	13D03-N07	3
Caelo	Betamethasone valerate	17078702	1
Caelo	Betamethasone valerate	17078711	4
Caelo	Betamethasone valerate	17329015	5
Caelo	Betamethasone valerate	15262603	14
Caelo	Betamethasone valerate	17078714	11
Caelo	Betamethasone valerate	13091210	3
Caelo	Betamethasone valerate	15398501	19
Caelo	Betamethasone valerate	16B18-B02-320971	1
Caelo	Betamethasone valerate	15/16-B07-317417	1
Caelo	Betamethasone valerate	1406019-01	1
Caelo	Betamethasone valerate	16270513	16
Caelo	Betamethasone valerate	12G09-N07	3
Caelo	Betamethasone valerate	15F16-B04-315327	1
Caelo	Betamethasone valerate	13225509	2
Caelo	Betamethasone valerate	13K29-B32-288247	1
Caelo	Betamethasone valerate	1406019-03	3
Caelo	Betamethasone valerate	BV-BLT225/0514	1
Caelo	Betamethasone valerate	1526213	1
Caelo	Betamethasone valerate	16270511	23
Caelo	Betamethasone valerate	16270508	1
Caelo	Betamethasone valerate	17078704	6
Caelo	Betamethasone valerate	1707819	1
Caelo	Betamethasone valerate	1819918	1
Caelo	Betamethasone valerate	17196001	1
Caelo	Betamethasone valerate	14188602	2
Caelo	Betamethasone valerate	12229813	2
Caelo	Betamethasone valerate	16E23-B03-324799	2

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Supplier	Substance	Batch	Spectra
Caelo	Betamethasone valerate	12229805	9
Caelo	Betamethasone valerate	13091203	12
Caelo	Betamethasone valerate	14G30-B05-309520	1
Caelo	Betamethasone valerate	140601903	1
Caelo	Betamethasone valerate	15262610	4
Caelo	Betamethasone valerate	16270509	6
Caelo	Betamethasone valerate	17078701	13
Caelo	Betamethasone valerate	17329001	11
Caelo	Betamethasone valerate	1739002	2
Caelo	Betamethasone valerate	18199918	6
Caelo	Betamethasone valerate	18199930	2
Fagron	Betamethasone valerate	17329016	1
Caelo	Betamethasone valerate	17K16-B08-345541	1
Caelo	Betamethasone valerate	12229812	9
Caelo	Betamethasone valerate	15B24-B04	1
Caelo	Betamethasone valerate	16E23-B03-324800	1
Caelo	Betamethasone valerate	16E23-B03-328128	3
Caelo	Betamethasone valerate	17C29-B04	2
Caelo	Betamethasone valerate	18199914	1
Caelo	Betamethasone valerate	17K16-B08	1
Caelo	Betamethasone valerate	18199926	1
Caelo	Betamethasone valerate	18199937	1
Caelo	Betamethasone valerate	2x12229813	1
Caelo	Betamethasone valerate	12L11-N01	1
Caelo	Betamethasone valerate	14188617	3
Caelo	Betamethasone valerate	15075803	7
Caelo	Betamethasone valerate	14H28-B01-302865	1
Caelo	Betamethasone valerate	150758022	1
Caelo	Betamethasone valerate	15B24-B04-307016	1
Caelo	Betamethasone valerate	1538506	1
Caelo	Betamethasone valerate	15395512	1
Caelo	Betamethasone valerate	16270503	15
Caelo	Betamethasone valerate	16270514	6
Caelo	Betamethasone valerate	17078703	20
Caelo	Betamethasone valerate	1708701	1
Caelo	Betamethasone valerate	17/251/Bv	1
Caelo	Betamethasone valerate	17078712	12
Caelo	Betamethasone valerate	17078713	15
Caelo	Betamethasone valerate	17078720	14
Caelo	Betamethasone valerate	17K16-B0/8-347310	1
Caelo	Betamethasone valerate	17K16-B08-347912	1
Caelo	Betamethasone valerate	17329019	3
Caelo	Betamethasone valerate	18199924	4
Caelo	Betamethasone valerate	15075812	3
Caelo	Betamethasone valerate	12g09-n07	1
Caelo	Betamethasone valerate	16E23-B03	1
Caelo	Betamethasone valerate	16270502	31
Caelo	Betamethasone valerate	15F16-B04-314054	1
Caelo	Betamethasone valerate	1707814	1
Caelo	Betamethasone valerate	11131905	1
Caelo	Betamethasone valerate	12229811	7
Caesar & Loretz	Betamethasone valerate	17329016	1
Caesar & Loretz GmbH	Betamethasone valerate	13225504	1
Caesar & Loretz GmbH	Betamethasone valerate	17078701	1
Caesar & Loretz GmbH	Betamethasone valerate	17329002	1
Caesar & Loretz GmbH	Betamethasone valerate	17K16B08345555	1
Caesar & Loretz GmbH	Betamethasone valerate	18199907	3
Caesar & Loretz GmbH	Betamethasone valerate	18199903	1
Caesar & Loretz GmbH	Betamethasone valerate	18199918	5
Caesar & Loretz GmbH	Betamethasone valerate	18199914	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Betamethasone valerate	18199923	1
Caesar & Loretz GmbH Hi...	Betamethasone valerate	120801402	1
Caesar & Loretz GmbH, 4...	Betamethasone valerate	10296707	1
Caesar & Loretz GmbH, 4...	Betamethasone valerate	12003404	1
Caesar & Loretz GmbH, 4...	Betamethasone valerate	12003409	2
Caesar & Loretz GmbH, 4...	Betamethasone valerate	12229809	1
Caesar & Loretz GmbH, 4...	Betamethasone valerate	13091206	2
Caesar & Loretz GmbH, 4...	Betamethasone valerate	13091211	1
Caesar & Loretz GmbH/Go...	Betamethasone valerate	18199918	1
Caesar & Loretz GmbH/Mi...	Betamethasone valerate	18199907	1
Caesar & Loretz GmbH/Mi...	Betamethasone valerate	18199908	1
Caesar & Loretz GmbH/Mi...	Betamethasone valerate	18199918	1
Caesar & Loretz/Gehe	Betamethasone valerate	18199932	1
Caesar & Loretz GmbH	Betamethasone valerate	11131917	1
Caesar und Loretz	Betamethasone valerate	15075803	1
Caesar&Loretz GmbH	Betamethasone valerate	15262609	1
Caesar&Loretz GmbH,PHön...	Betamethasone valerate	16270509	1
Caesar&Loretz GmbH/Anzag	Betamethasone valerate	15075802	1
caesar&lorenz,phönix	Betamethasone valerate	14188606	1
Caesar/Lorenz	Betamethasone valerate	12003403	1
Caleo/Phönix	Betamethasone valerate	1522609	1
Cealo	Betamethasone valerate	17078716	1
Cealo/Gehe	Betamethasone valerate	1801024-01	1
Cealo/Gehe	Betamethasone valerate	17329002	1
Cealo/Gehe	Betamethasone valerate	1739002	1
Cealo/Noweda	Betamethasone valerate	16270509	2
E Plus	Betamethasone valerate	16270502	1
E Plus	Betamethasone valerate	17329002	1
Ebert u. Jacobi 16.0...	Betamethasone valerate	15/16-B07-317417	1
Eigenherstellung	Betamethasone valerate	9070313	1
Euro OTC	Betamethasone valerate	120801402	2
Eurho	Betamethasone valerate	1801024-01	1
EuRho	Betamethasone valerate	1208014-02	1
EuRho	Betamethasone valerate	1208014-01	1
EuRho	Betamethasone valerate	180102401	1
EuRho	Betamethasone valerate	1801024-01	3
EuRho	Betamethasone valerate	181008-01	1
EuRho / Phoenix	Betamethasone valerate	1704019-01	1
Euro OTC	Betamethasone valerate	110804-02	1
Euro	Betamethasone valerate	1406019-03	3
Euro	Betamethasone valerate	1801024-01	2
Euro OTC	Betamethasone valerate	14C19-B02-292650	2
Euro OTC	Betamethasone valerate	151003701	1
Euro OTC	Betamethasone valerate	161001001	1
Euro OTC	Betamethasone valerate	120812-02	1
Euro OTC	Betamethasone valerate	110804503	1
Euro OTC	Betamethasone valerate	1208014-03	4
Euro OTC	Betamethasone valerate	1208014-04	4
Euro OTC	Betamethasone valerate	120801403	1
Euro OTC	Betamethasone valerate	1311039-01	22
Euro OTC	Betamethasone valerate	131103901	1
Euro OTC	Betamethasone valerate	1406019-02	23
Euro OTC	Betamethasone valerate	140601902	1
Euro OTC	Betamethasone valerate	1510037-01	20
Euro OTC	Betamethasone valerate	15/16-B07-319228	1
Euro OTC	Betamethasone valerate	16100100-01	1
Euro OTC	Betamethasone valerate	16E23-B03-328128	3
Euro OTC	Betamethasone valerate	1704019	2
Euro OTC	Betamethasone valerate	17078703	1
Euro OTC	Betamethasone valerate	17C29-B04-336434	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Betamethasone valerate	29061805	1
Euro OTC	Betamethasone valerate	7071802	1
Euro OTC	Betamethasone valerate	1801024-01	72
Euro OTC	Betamethasone valerate	1610010-01	41
Euro OTC	Betamethasone valerate	1801024_01	1
Euro OTC	Betamethasone valerate	1704019-01	95
Euro OTC	Betamethasone valerate	1704018-01	1
Euro OTC	Betamethasone valerate	13D03-N07	1
Euro OTC	Betamethasone valerate	120801404	1
Euro OTC	Betamethasone valerate	1031707	1
Euro OTC	Betamethasone valerate	170419-01	1
Euro OTC	Betamethasone valerate	1108045-01	2
Euro OTC	Betamethasone valerate	1108045-02	3
Euro OTC	Betamethasone valerate	1108045-03	7
Euro OTC	Betamethasone valerate	1704019-1	1
Euro OTC	Betamethasone valerate	1704019-0	1
Euro OTC	Betamethasone valerate	1811008-01	13
Euro OTC	Betamethasone valerate	1740419-01	1
Euro OTC	Betamethasone valerate	131139-01	1
Euro OTC	Betamethasone valerate	1208014-02	11
Euro OTC	Betamethasone valerate	1704019-01	1
Euro OTC	Betamethasone valerate	3313U-01181	1
Euro OTC	Betamethasone valerate	2014Q1181	1
Euro OTC	Betamethasone valerate	17078720	1
Euro OTC	Betamethasone valerate	1704019_01	1
Euro OTC	Betamethasone valerate	1311039	1
Euro OTC	Betamethasone valerate	140601901	1
Euro OTC	Betamethasone valerate	140601903	2
Euro OTC	Betamethasone valerate	1406019-03	28
Euro OTC	Betamethasone valerate	1406011903	1
Euro OTC	Betamethasone valerate	12L11-N01	1
Euro OTC	Betamethasone valerate	1206014-02	1
Euro OTC	Betamethasone valerate	1606023-01	34
Euro OTC	Betamethasone valerate	170401901	3
Euro OTC	Betamethasone valerate	181100801	3
Euro OTC	Betamethasone valerate	1811008-1	1
Euro OTC	Betamethasone valerate	15398501	1
Euro OTC	Betamethasone valerate	17K16-B08-345541	1
euro//Noweda	Betamethasone valerate	1801024-01	2
Euro/Alliance Healthcare	Betamethasone valerate	1510037-01	1
Euro/direkt	Betamethasone valerate	1704019-01	1
Euro/Gehe	Betamethasone valerate	1704019-01	1
Euroo	Betamethasone valerate	1406019-03	1
Euro OTC	Betamethasone valerate	13K29-B32-289364	1
Euro OTC	Betamethasone valerate	180102401	2
Euro OTC	Betamethasone valerate	1516B07317416	1
Euro OTC	Betamethasone valerate	BV116/1117	1
Euro OTC	Betamethasone valerate	BV-BLT221/0314	1
Europ Ots Pharma	Betamethasone valerate	12111-N01	1
EurRho/Gehe	Betamethasone valerate	1610010-01	1
Fagron	Betamethasone valerate	15075802	1
Fagron	Betamethasone valerate	B07-317416	1
Fagron	Betamethasone valerate	NP1351M	1
Fagron	Betamethasone valerate	12B28-N01	8
Fagron	Betamethasone valerate	612211181	1
Fagron	Betamethasone valerate	20101012-1	1
Fagron	Betamethasone valerate	11A04-N02	1
Fagron	Betamethasone valerate	12L11-N01	18
Fagron	Betamethasone valerate	2B28-N01	1
Fagron	Betamethasone valerate	13d03-n07	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Betamethasone valerate	13G19-N01	49
Fagron	Betamethasone valerate	NT0597M	3
Fagron	Betamethasone valerate	13G19N01	1
Fagron	Betamethasone valerate	13G19-N01	1
Fagron	Betamethasone valerate	11E18-N03	3
Fagron	Betamethasone valerate	NT059M	1
Fagron	Betamethasone valerate	13K29-B32-288250	3
Fagron	Betamethasone valerate	13K29B32	1
Fagron	Betamethasone valerate	13K29-B32-288244	2
Fagron	Betamethasone valerate	13K29-B12-288247	1
Fagron	Betamethasone valerate	14C19-B02-292653	6
Fagron	Betamethasone valerate	13K29-B32-288248	3
Fagron	Betamethasone valerate	14C19-B02-292650	4
Fagron	Betamethasone valerate	14C19-B02-296169	1
Fagron	Betamethasone valerate	14c19-b02-292650	1
Fagron	Betamethasone valerate	13K05-B08-092652	1
Fagron	Betamethasone valerate	13K29-B32-288245	1
Fagron	Betamethasone valerate	14C19-B02-296168	4
Fagron	Betamethasone valerate	14G30-B05-296172	3
Fagron	Betamethasone valerate	14H28-B01-302866	6
Fagron	Betamethasone valerate	14C19B02	1
Fagron	Betamethasone valerate	14G30B05309519	1
Fagron	Betamethasone valerate	14H28B01	1
Fagron	Betamethasone valerate	14G30-B05-309519	1
Fagron	Betamethasone valerate	14G30-B05-29617	1
Fagron	Betamethasone valerate	14H28-B01-302863	4
Fagron	Betamethasone valerate	12K07N23	1
Fagron	Betamethasone valerate	14H28-b01-302866	1
Fagron	Betamethasone valerate	309520	1
Fagron	Betamethasone valerate	14G30-B05-309528	1
Fagron	Betamethasone valerate	14h28-b01-302865	2
Fagron	Betamethasone valerate	14G30-B05-309521	1
Fagron	Betamethasone valerate	14H28-B01-302877	3
Fagron	Betamethasone valerate	15824-B04	1
Fagron	Betamethasone valerate	1406019-03	1
Fagron	Betamethasone valerate	15I16-B07-317417	1
Fagron	Betamethasone valerate	15/16-B07-317417	2
Fagron	Betamethasone valerate	14H28-B01-305470	1
Fagron	Betamethasone valerate	90616-2	1
Fagron	Betamethasone valerate	15F16-B04-315328	3
Fagron	Betamethasone valerate	15F16-804-314054	1
Fagron	Betamethasone valerate	15/16-B07-319228	3
Fagron	Betamethasone valerate	1526260	1
Fagron	Betamethasone valerate	16B18-B02-322121	3
Fagron	Betamethasone valerate	16B18-B02-323034	3
Fagron	Betamethasone valerate	15/16-B07-319832	1
Fagron	Betamethasone valerate	15116-B07-319832	2
Fagron	Betamethasone valerate	16B18-B02	5
Fagron	Betamethasone valerate	11K-18-N09	1
Fagron	Betamethasone valerate	15398515	1
Fagron	Betamethasone valerate	16B18-B02-323033	1
Fagron	Betamethasone valerate	16E23-B03	7
Fagron	Betamethasone valerate	15I16-Bo7-319832	1
Fagron	Betamethasone valerate	15/16-B07	1
Fagron	Betamethasone valerate	17C29-B04-333688	1
Fagron	Betamethasone valerate	16H22-B06-330524	4
Fagron	Betamethasone valerate	16H22-B06-330523	3
Fagron	Betamethasone valerate	1704019-01	3
Fagron	Betamethasone valerate	16E23-B03-327350	3
Fagron	Betamethasone valerate	16H22-B06-332351	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Betamethasone valerate	17C29-335654	1
Fagron	Betamethasone valerate	16E23-B03-3247990855	1
Fagron	Betamethasone valerate	17C29-B04-335658	1
Fagron	Betamethasone valerate	17C29-B04-33368	1
Fagron	Betamethasone valerate	17C29-B04-336434	4
Fagron	Betamethasone valerate	17C29-B04	4
Fagron	Betamethasone valerate	17G31-B04-339784	6
Fagron	Betamethasone valerate	17g31-b04-341576	3
Fagron	Betamethasone valerate	BV109/0117	1
Fagron	Betamethasone valerate	17G31-B04-339785	3
Fagron	Betamethasone valerate	17K16-B08	8
Fagron	Betamethasone valerate	17k16-b08-345541	4
Fagron	Betamethasone valerate	17K16-B08-344754	3
Fagron	Betamethasone valerate	17K16-B08-347912	3
Fagron	Betamethasone valerate	17G31B04339785	1
Fagron	Betamethasone valerate	17k16-B08-347309	1
Fagron	Betamethasone valerate	17K16-B08-348538	1
Fagron	Betamethasone valerate	18G03-B03-351450	5
Fagron	Betamethasone valerate	18G03-B03-351513	1
Fagron	Betamethasone valerate	17g31-b04-338575	1
Fagron	Betamethasone valerate	18G03-B03-351731	6
Fagron	Betamethasone valerate	BV124/0118	2
Fagron	Betamethasone valerate	18I27-B05-354898	1
Fagron	Betamethasone valerate	18/27-B05	1
Fagron	Betamethasone valerate	18G03-B03-351451	1
Fagron	Betamethasone valerate	18/27-B05-356570	1
Fagron	Betamethasone valerate	17G-31-B04-341576	1
Fagron	Betamethasone valerate	18I27-b05-358065	1
Fagron	Betamethasone valerate	17K16_B08-348042	1
Fagron	Betamethasone valerate	19G30-B02	3
Fagron	Betamethasone valerate	BV109/0519	1
Fagron	Betamethasone valerate	16818-B02-320971	1
Fagron	Betamethasone valerate	17K16-B08-347309	3
Fagron	Betamethasone valerate	17G31-B04-342639	1
Fagron	Betamethasone valerate	17K16-B08-349774	1
Fagron	Betamethasone valerate	14G30-B05-309520	6
Fagron	Betamethasone valerate	16E23-B03-327354	3
Fagron	Betamethasone valerate	14G31-B04-342639	1
Fagron	Betamethasone valerate	15F16-B04-314054/201	1
Fagron	Betamethasone valerate	14H28-B01-302864/201	1
Fagron	Betamethasone valerate	NS0706M	3
Fagron	Betamethasone valerate	13k29b32288247	1
Fagron	Betamethasone valerate	700103-0004	2
Fagron	Betamethasone valerate	16e23-b03-324800	1
Fagron	Betamethasone valerate	17C29-B04-335654	2
Fagron	Betamethasone valerate	17B14-B04	1
Fagron	Betamethasone valerate	13K29-B23-288246	1
Fagron	Betamethasone valerate	17C29-B04-334329	8
Fagron	Betamethasone valerate	17271604	2
Fagron	Betamethasone valerate	14G30-B05	3
Fagron	Betamethasone valerate	16B18-B02-322111	1
Fagron	Betamethasone valerate	17G31B04338575	1
Fagron	Betamethasone valerate	17G31-B04-341576-201	1
Fagron	Betamethasone valerate	BV-BLT250/0616	1
Fagron	Betamethasone valerate	13K29-B32-28824	1
Fagron	Betamethasone valerate	16H22-B06-329223	3
Fagron	Betamethasone valerate	15B24-B04-307015	3
Fagron	Betamethasone valerate	18G03-B03-352460	3
Fagron	Betamethasone valerate	18G03-B03-352458	1
Fagron	Betamethasone valerate	17K16-B08-345555	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Betamethasone valerate	18199907	1
Fagron	Betamethasone valerate	18127-B05-356584	1
Fagron	Betamethasone valerate	13K29B32288243	1
Fagron	Betamethasone valerate	15116-B07	1
Fagron	Betamethasone valerate	13117-B08-292649	2
Fagron	Betamethasone valerate	17c29-b04-335657	2
Fagron	Betamethasone valerate	14c19-b02-296169	1
Fagron	Betamethasone valerate	14C19-B02	3
Fagron	Betamethasone valerate	15F16-B04	2
Fagron	Betamethasone valerate	18G03-B03_351731	1
Fagron	Betamethasone valerate	19G30-B02-363693	1
Fagron	Betamethasone valerate	15I16-B07	1
Fagron	Betamethasone valerate	15I16B07317417	1
Fagron	Betamethasone valerate	17K16-B08-345541	8
Fagron	Betamethasone valerate	19G30-B02-363673	1
Fagron	Betamethasone valerate	17C29-B04-335657	7
Fagron	Betamethasone valerate	14G30-B05-296173	12
Fagron	Betamethasone valerate	15F16-B04-314882	1
Fagron	Betamethasone valerate	19I26-F02-364981	1
Fagron	Betamethasone valerate	14H28-B01-302865	13
Fagron	Betamethasone valerate	12G09-N07	23
Fagron	Betamethasone valerate	14H28-B01-302864	5
Fagron	Betamethasone valerate	16E23-B03-324799	7
Fagron	Betamethasone valerate	17G31-B04-344757	2
Fagron	Betamethasone valerate	13g19-n01	2
Fagron	Betamethasone valerate	13K05-B08-292652	1
Fagron	Betamethasone valerate	16H22-B06	3
Fagron	Betamethasone valerate	17K16-B08-347310	2
Fagron	Betamethasone valerate	14G30-B05-309518	2
Fagron	Betamethasone valerate	15/16-B07-317416	3
Fagron	Betamethasone valerate	16B18-B02-320971	5
Fagron	Betamethasone valerate	16E23-B03-324800	8
Fagron	Betamethasone valerate	16B18-B02-322109	5
Fagron	Betamethasone valerate	17G31-B04-341576	9
Fagron	Betamethasone valerate	BV036/1215	1
Fagron	Betamethasone valerate	13K29-B32-288246	5
Fagron	Betamethasone valerate	13K29-B32	6
Fagron	Betamethasone valerate	13K05-B08	2
Fagron	Betamethasone valerate	16B18-B02320971	2
Fagron	Betamethasone valerate	BV008/045	1
Fagron	Betamethasone valerate	17K16-B08-345542	1
Fagron	Betamethasone valerate	18G03-B03	5
Fagron	Betamethasone valerate	17k16-b08	1
Fagron	Betamethasone valerate	19G30-B02-363692	1
Fagron	Betamethasone valerate	15F16-B04-314054	4
Fagron	Betamethasone valerate	18I27-B05-356570	1
Fagron	Betamethasone valerate	292652	1
Fagron	Betamethasone valerate	15I16-B07-317416	1
Fagron	Betamethasone valerate	16E23-B03-328128	9
Fagron	Betamethasone valerate	11K18-N09	2
Fagron	Betamethasone valerate	15F16-B04-314055	1
Fagron	Betamethasone valerate	14C19-B02-292646	1
Fagron	Betamethasone valerate	13K05-B08-291663	1
Fagron	Betamethasone valerate	BV019/0514	3
Fagron	Betamethasone valerate	14188603	1
Fagron	Betamethasone valerate	BV-BLT225/0514	1
Fagron	Betamethasone valerate	15f16-b04314054	1
Fagron	Betamethasone valerate	15I16-B07-319228	2
Fagron	Betamethasone valerate	16b18-b02-324798	1
Fagron	Betamethasone valerate	16270513	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Betamethasone valerate	BV106/0717	2
Fagron	Betamethasone valerate	17329001	1
Fagron	Betamethasone valerate	18I27-B05	3
Fagron	Betamethasone valerate	18/27-B05-356571	1
Fagron	Betamethasone valerate	17G31-B04-3415765	1
Fagron	Betamethasone valerate	700103-0002	1
Fagron	Betamethasone valerate	NS2072M	1
Fagron	Betamethasone valerate	14H28-B01	3
Fagron	Betamethasone valerate	14C19B02296168	1
Fagron	Betamethasone valerate	15B24-B04-307016	12
Fagron	Betamethasone valerate	15B24-B04	1
Fagron	Betamethasone valerate	1516-B07-317416	1
Fagron	Betamethasone valerate	BV008/0516	1
Fagron	Betamethasone valerate	16b18-b02-323034	1
Fagron	Betamethasone valerate	17G31-B04	3
Fagron	Betamethasone valerate	17G31B04341576	1
Fagron	Betamethasone valerate	17329008	1
Fagron	Betamethasone valerate	17K16-B0B-345541	1
Fagron	Betamethasone valerate	19G30-B02-363672	1
Fagron	Betamethasone valerate	16e23b03324800	1
Fagron	Betamethasone valerate	13D03-N07	38
Fagron	Betamethasone valerate	12L11-N01	1
Fagron	Betamethasone valerate	14C19-B02-292648	1
Fagron	Betamethasone valerate	15I16-B07-319832	3
Fagron	Betamethasone valerate	16818-B02-323033	1
Fagron	Betamethasone valerate	16E23B03328128	1
Fagron	Betamethasone valerate	16H22-B06-330522	2
Fagron	Betamethasone valerate	16h22-b06-330523	2
Fagron	Betamethasone valerate	17c29-b04-335654	1
Fagron	Betamethasone valerate	17G31-B-04	1
Fagron	Betamethasone valerate	18/27-B05-354880	1
Fagron	Betamethasone valerate	18G03-B03-351730	1
Fagron	Betamethasone valerate	1811008-01	1
Fagron	Betamethasone valerate	14H28-B01-302683	1
Fagron	Betamethasone valerate	13K05-B08-292647	2
Fagron	Betamethasone valerate	14G30-B05-296175	2
Fagron	Betamethasone valerate	BV008/0415	1
Fagron	Betamethasone valerate	17C29B043356575581	1
Fagron	Betamethasone valerate	17K-16-B08-347309	2
Fagron	Betamethasone valerate	17K16-B08-349755	6
Fagron	Betamethasone valerate	18G03-B03-353212	1
Fagron	Betamethasone valerate	15/16-B07-317428	3
Fargon	Betamethasone valerate	13k29-b32-289364	1
Fargon	Betamethasone valerate	7890	1
Fargon, Noweda 07.11.2017	Betamethasone valerate	16H22-B06-329223	1
Fargon/Alliance HC	Betamethasone valerate	13K29-B32-288247	1
Fargon/Alliance HC	Betamethasone valerate	16B18-B02-322111	1
Fargon/Anzag	Betamethasone valerate	13G19-N01	1
Fargon/Anzag	Betamethasone valerate	16B18-B02-320971	1
Farmabios S. p. A./ Now...	Betamethasone valerate	17078715	1
Fiebig	Betamethasone valerate	14H28-B01	1
Fiebig	Betamethasone valerate	15B24-B04-307016	1
Fiebig	Betamethasone valerate	16B18-B02-322111	1
Fiebig	Betamethasone valerate	17271603	1
Fiebig 27.06.13 EK47,81	Betamethasone valerate	B9/131	1
Fiebig ek: 45,65EUR	Betamethasone valerate	12B28-N01	1
Finteler Apotheke	Betamethasone valerate	17C29-B04-333688	2
Fragon/Alliance	Betamethasone valerate	17k16-B08	1
Fragon/Phönix	Betamethasone valerate	17G31-B04-341576	1
Fragron	Betamethasone valerate	BV-BLT225/0514	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Galderma/ Noweda	Betamethasone valerate	C0023/115040	1
Gatt-Koller	Betamethasone valerate	1800117	1
Gehe	Betamethasone valerate	12003403	1
Gehe	Betamethasone valerate	12003409	1
Gehe	Betamethasone valerate	12229809	1
Gehe	Betamethasone valerate	1208014-04	1
Gehe	Betamethasone valerate	13091211	1
Gehe	Betamethasone valerate	1712E-01181	1
Gehe	Betamethasone valerate	14H28-B01-302863	1
Gehe	Betamethasone valerate	14H25-B01-302863	1
Gehe	Betamethasone valerate	15398501	1
Gehe	Betamethasone valerate	16270505	1
Gehe	Betamethasone valerate	16H22-B06-330524	1
Gehe	Betamethasone valerate	17G31-B04	1
Gehe	Betamethasone valerate	17K16-B08-347309	1
Gehe	Betamethasone valerate	17K16-B08	1
Gehe	Betamethasone valerate	17K16-B08-348042	1
Gehe	Betamethasone valerate	18G03-B03-351731	1
Gehe	Betamethasone valerate	1811008-01	1
Gehe	Betamethasone valerate	18199924	2
GEHE	Betamethasone valerate	16270501	1
GEHE	Betamethasone valerate	17078701	2
GEHE	Betamethasone valerate	17078719	1
GEHE	Betamethasone valerate	17078720	1
GEHE	Betamethasone valerate	18199902	2
Fagron	Betamethasone valerate	14G30B05296172	1
GEHE 17.06.2014	Betamethasone valerate	13225503	1
Gehe am 03.02.2014	Betamethasone valerate	13091210	3
Caelo	Betamethasone valerate	1627051	1
Caelo	Betamethasone valerate	12003402	1
Fagron	Betamethasone valerate	120801402	1
Fagron	Betamethasone valerate	14G30-Bo5-296172	1
Fagron	Betamethasone valerate	16B18B02320971	1
Fagron	Betamethasone valerate	16H22B06330524	2
Fagron	Betamethasone valerate	BV009/0117	1
Fagron	Betamethasone valerate	17K16-B08-348042	7
Hedinger	Betamethasone valerate	14H28-B01-302877	1
Klenk	Betamethasone valerate	16623-01	1
Hepart AG, CH-8280 Kreu...	Betamethasone valerate	11131914	3
Hirsch	Betamethasone valerate	13G19-No1	1
Holdermann	Betamethasone valerate	1208014-01	1
Holdermann	Betamethasone valerate	120801402	1
Ichthyol-Gesellschaft	Betamethasone valerate	13k29-B32-288247	1
Ichthyol-Gesellschaft	Betamethasone valerate	17078720	1
Jenne	Betamethasone valerate	17078712	1
Kehr	Betamethasone valerate	1801024-01	1
Klenk	Betamethasone valerate	17078713	1
Klosterring	Betamethasone valerate	18199916	2
Fagron	Betamethasone valerate	17G-31-B04-339784	1
Euro OTC	Betamethasone valerate	160623-01	1
L12	Betamethasone valerate	16E23-B03-324799	2
L12	Betamethasone valerate	17C29-B04-334329	2
L12	Betamethasone valerate	17K16-B08-345541	1
Caelo	Betamethasone valerate	BV018/0715	2
Fagron	Betamethasone valerate	16B18-B02-324798	3
Midas	Betamethasone valerate	16270503	1
Midas	Betamethasone valerate	16270513	1
Midas	Betamethasone valerate	17078712	2
Midas	Betamethasone valerate	17G31-B04-338575	2
Midas	Betamethasone valerate	17078720	1

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Supplier	Substance	Batch	Spectra
Midas	Betamethasone valerate	17329001	2
Midas	Betamethasone valerate	17329018	1
NEWCHEM	Betamethasone valerate	1311039-01	1
Noveda	Betamethasone valerate	1311039-01	1
noweda	Betamethasone valerate	1208014-04	1
noweda	Betamethasone valerate	1406019-01	1
Noweda	Betamethasone valerate	11131902	1
Noweda	Betamethasone valerate	12G09-N07	1
Noweda	Betamethasone valerate	11B21-N02	1
Noweda	Betamethasone valerate	1208014-02	2
Noweda	Betamethasone valerate	12229832	1
Noweda	Betamethasone valerate	1208014-01	1
Noweda	Betamethasone valerate	13091203	1
Noweda	Betamethasone valerate	13091205	1
Noweda	Betamethasone valerate	15075812	1
Noweda	Betamethasone valerate	14H28B01302863	1
Noweda	Betamethasone valerate	1406019-03	2
Noweda	Betamethasone valerate	BV01090117	1
Noweda	Betamethasone valerate	17329018	2
Noweda	Betamethasone valerate	18127-B05-354880	1
Noweda	Betamethasone valerate	18199932	3
Caelo	Betamethasone valerate	13091211	3
Caelo	Betamethasone valerate	15262604	12
Noweda/ Infecto Pharm	Betamethasone valerate	16270505	1
Caelo	Betamethasone valerate	13225502	2
Caelo	Betamethasone valerate	13225515	8
Noweda/Ceasar Lorenz	Betamethasone valerate	14188606	1
Fagron	Betamethasone valerate	13/17-B08-292649	2
Fagron	Betamethasone valerate	14H28B01302864	1
Fagron	Betamethasone valerate	17C29-B04-335676	6
Fagron	Betamethasone valerate	16H22-B06-329231	4
Oberlinden Apotheke	Betamethasone valerate	C0073/115040	3
Oberlinden Apotheke	Betamethasone valerate	c073/115040	1
Oberlinden- Apotheke	Betamethasone valerate	C0073/1	3
Euro OTC	Betamethasone valerate	2507211181	1
Fagron	Betamethasone valerate	16E23-B03-328129	2
Phoenix	Betamethasone valerate	12003409	2
Phoenix	Betamethasone valerate	17C29-B04-334329	1
Phoenix	Betamethasone valerate	3105	1
Phoenix	Betamethasone valerate	17K16-B08-348042	2
Phoenix	Betamethasone valerate	17329018	1
Phoenix	Betamethasone valerate	3364	1
Phoenix	Betamethasone valerate	1801024-01	1
Phoenix	Betamethasone valerate	18127-B05-358065	1
Phoenix	Betamethasone valerate	19G30-B02-363672	2
Phoenix	Betamethasone valerate	1811008-01	2
Phoenix	Betamethasone valerate	19G30-B02-363682	1
Phoenix 15.1.2014	Betamethasone valerate	1208014-04	1
Phoenix 22.01.2019	Betamethasone valerate	1801021-01	1
Phoenix Goettin	Betamethasone valerate	13225508	1
Phoenix/ Fagro	Betamethasone valerate	18G03-B03-351731	1
Caelo	Betamethasone valerate	12003406	6
Caelo	Betamethasone valerate	15262607	7
Phonix	Betamethasone valerate	13K29-B32	1
phönix	Betamethasone valerate	15/16B07-319228	1
phönix	Betamethasone valerate	15398515	1
phönix	Betamethasone valerate	16e23-b03-327350	1
Phönix	Betamethasone valerate	12229807	1
Phönix	Betamethasone valerate	13091201	2
Phönix	Betamethasone valerate	13D03-N07	1

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Supplier	Substance	Batch	Spectra
Phönix	Betamethasone valerate	BV-BLT186/0512	1
Phönix	Betamethasone valerate	13091209	2
Phönix	Betamethasone valerate	13091212	2
Phönix	Betamethasone valerate	16H22-B06-330522	1
Phönix	Betamethasone valerate	BV110/0818	1
Phönix	Betamethasone valerate	19I26-F02-364981	1
Fagron	Betamethasone valerate	18I27-B05-358065	1
Phönix Gotha	Betamethasone valerate	12229808	1
Phönix Gotha	Betamethasone valerate	13091213	1
Phönix Gotha	Betamethasone valerate	14188608	1
Phönix WE:16.07.2016 ...	Betamethasone valerate	1510037-01	1
Caelo	Betamethasone valerate	1208014-01	1
Fagron	Betamethasone valerate	1311039-01	1
Fagron	Betamethasone valerate	17G31-B04-338575	8
Sanacorp	Betamethasone valerate	12G09-N07	1
Sanacorp	Betamethasone valerate	30051201	1
Sanacorp	Betamethasone valerate	13091210	1
Sanacorp	Betamethasone valerate	14188602	1
Sanacorp	Betamethasone valerate	17C29-B04	1
Sanacorp	Betamethasone valerate	17078719	1
Sanacorp	Betamethasone valerate	17078715	1
Caelo	Betamethasone valerate	1811008-01	2
Sanacorp W.E: 18.01.18 ...	Betamethasone valerate	1704019-01	1
Caelo	Betamethasone valerate	11131917	2
Caelo	Betamethasone valerate	12003403	7
Caelo	Betamethasone valerate	12003405	8
Spangro	Betamethasone valerate	17078714	1
Fagron	Betamethasone valerate	13K29-B32-288247	18
Spangro 31.05.2013	Betamethasone valerate	13D03-N07	2
Spangro_21.05.2019	Betamethasone valerate	1811008-01	3
Symbiotica	Betamethasone valerate	1610010-01	2
Symbiotica	Betamethasone valerate	14H28B01302863	1
Symbiotica Spec.	Betamethasone valerate	1208014-04	1
Symbiotica Spec.	Betamethasone valerate	1406019-01	3
Symbiotica/ Anzag	Betamethasone valerate	1606023-01	2
Symbiotica Spec/Noweda	Betamethasone valerate	1208014-04	1
vdl	Betamethasone valerate	12003411	1
	Betamethasone valerate	1208014-04	1
Caelo	Betamethasone valerate	13091213	6
Caelo	Betamethasone valerate		1
Caelo	Betamethasone valerate	13225507	2
Euro OTC	Betamethasone valerate	1208014-01	12
Euro OTC	Betamethasone valerate	1406019-01	24
Euro OTC	Betamethasone valerate	1510037	1
Euro OTC	Betamethasone valerate	1811008	1
Fagron	Betamethasone valerate	12K07-N23	6
Sanacorp	Betamethasone valerate		1

- 108 695 spectra from 742 *Apo-Ident* customers from a total of 31 375 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Betamethasone valerate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this

purpose, all relevant spectra of the various substances were compared with *Betamethasone valerate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	554	0	110 135
Type B	0	459	0	118 683
Type C	0	2536	16	108 695

The substance/substance group *Betamethasone valerate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9170 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.6928 %)
Type C	100.0000 % (> 99.8899 %)	99.3730 % (> 99.2555 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Betamethasone valerate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisolon dihydrogen phosphate dinat...	19.17	—
Dexamethasone acetate	19.71	—
Dexamethasone	19.91	60.01
Ciclosporin	30.05	—
Budesonide, micronized	32.96	58.16
Clobetasol propionate	33.19	—
Prednicarbate, micronized	34.80	56.08
Erythromycin	34.89	63.28
Triamcinolone acetonide	34.95	34.40
Prednisolone hydrogen succinate	38.79	—
Estradiol valerate	46.43	—
Betamethasone dipropionate, micronized	48.93	—
⋮	⋮	⋮
Prednisolone, micronized	>50	71.48
Prednisone	>50	132.80
Triamcinolone, micronized	>50	137.12
Betamethasone, micronized	>50	148.65
Norethisterone acetate	>50	165.33
Capsaicin	>50	167.48
Heparin sodium	>50	239.87

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Betamethasone valerate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22861	22861	0.00	20.18
21588	21588	0.00	24.40
24349	24349	0.00	21.33
21674	21674	0.00	19.71
21645	22249	2.87	21.64
22249	22249	0.00	20.16
20887	22249	4.35	21.86
21215	22249	3.03	20.07
20920	22861	4.88	20.44
21566	22249	3.88	19.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Betamethasone, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20943-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Betamethasone, micronized; Betamethasonum, micronisatum

Special notes

When selecting the *Betamethasone, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Betamethasone, micronized	3	2	22

Second-stage model

For differentiation of the substance/substance group *Betamethasone, micronized* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Betamethasone, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Betamethasone, m...	12D26-N08	20943	40	1402096
Fagron	Betamethasone, m...	13H08-N06	21579	60	1411037
Fagron	Betamethasone, m...	11H31-B06-288219	22493	40	1608324

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Betamethasone, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Betamethasone, micronized*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Betamethasone, micronized	14C13-B02-296165	22897	40
Fagron	Betamethasone, micronized	15L09-B05-324091	22904	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 31 spectra from 21 *Apo-Ident* customers from 23 batches from the substance/substance group *Betamethasone, micronized*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
BASF/Phönix	Betamethasone, micronized	ZBtBY13004	1
Caelo	Betamethasone, micronized	16107-B01-341871	1
Caelo	Betamethasone, micronized	11/14-N02	1
Fagron	Betamethasone, micronized	12B20-N05	2
Fagron	Betamethasone, micronized	11/14-N02	1
Fagron	Betamethasone, micronized	9071304	1
Fagron	Betamethasone, micronized	14C13-B02-296164	2
Fagron	Betamethasone, micronized	12D26-N08	1
Fagron	Betamethasone, micronized	14C13-B02-296154	1
Fagron	Betamethasone, micronized	14c13-b02-305561	1
Fagron	Betamethasone, micronized	15L09-B05	1
Fagron	Betamethasone, micronized	ZBTBY15002	1
Fagron	Betamethasone, micronized	16I07-B01-341871	2
Fagron	Betamethasone, micronized	12J01-N02	1
Fagron	Betamethasone, micronized	15L09-B05_322119	1
Fagron	Betamethasone, micronized	9J26-N08	1
Fagron	Betamethasone, micronized	9K25-N13	1
Fagron	Betamethasone, micronized	14C13-B02	2
Fagron	Betamethasone, micronized	14C13-B02-305561	1
Fiebig	Betamethasone, micronized	12J01-120301-m1	1
Noweda	Betamethasone, micronized	12B20-N05	1
Noweda	Betamethasone, micronized	M-X01-120301m1	1
Fagron	Betamethasone, micronized	11H31-B06-288217	1
Phönix	Betamethasone, micronized	12B20-N05	1
Symbiotec Pharmed Lab Ltd. ...	Betamethasone, micronized	14C13-B02	1
Unisan	Betamethasone, micronized	Retest09K25-N13	1
Fagron	Betamethasone, micronized	12D26-N08	1

- 111 216 spectra from 742 *Apo-Ident* customers from a total of 31 868 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Betamethasone, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Betamethasone, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	19	12	111 216

The substance/substance group *Betamethasone, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	61.2903 % (> 51.6129 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Betamethasone, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Triamcinolone acetonide	19.19	58.00
Prednisolone, micronized	22.42	85.40
Dexamethasone	25.97	35.29
Dexamethasone acetate	31.99	—
Prednisolon dihydrogen phosphate dinat...	32.11	—
Fluocinoloneacetonid, micronized	33.08	—
Methylprednisolone	37.59	—
Sodium edetate	39.73	—
Cyanocobalamin	43.78	—
Prednisolone acetate	49.28	—
⋮	⋮	⋮
Triamcinolone, micronized	>50	68.55
Erythromycin	>50	77.41
Capsaicin	>50	97.39
Betamethasone valerate	>50	107.16
Budesonide, micronized	>50	109.89
Prednisone	>50	134.90
Prednicarbate, micronized	>50	137.51

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Substanz	Distance in main model	Distance in second-stage model
Heparin sodium	>50	296.16
Norethisterone acetate	>50	316.03

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Betamethasone, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22493	22493	0.00	22.32
21579	21579	0.00	22.42
20943	20943	0.00	19.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Bifonazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20810-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bifonazole; Bifonazolum

Special notes

When selecting the *Bifonazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Bifonazole	8	3	37

Second-stage model

For differentiation of the substance/substance group *Bifonazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Bifonazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Bifonazole	15152701	22906	40	20150703
Caelo	Bifonazole	15152702	22907	40	20150703
Caelo	Bifonazole	15152702	22955	40	20150703
Caelo	Bifonazole	151527	23364	40	20150703*
Euro OTC	Bifonazole	1206027-01	20810	40	1312397
Euro OTC	Bifonazole	1401031-01	21631	60	20140220
Euro OTC	Bifonazole	1510001	22253	60	20151203*
Fagron	Bifonazole	12G11-N09	20820	40	20120807
Fagron	Bifonazole	16D07-B10-324381	22941	40	20160419

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 9 reference samples from the substance/substance group *Bifonazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 289 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 180 spectra of 4 reference samples from the substance/substance group *Bifonazole*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Bifonazole	182771	24365	40
Euro OTC	Bifonazole	1703041	23395	40
Euro OTC	Bifonazole	1806008	24161	40
Euro OTC	Bifonazole	1510001	2225381 [†]	60

- 118 962 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 86 spectra from 42 *Apo-Ident* customers from 43 batches from the substance/substance group *Bifonazole*.
- Among them are spectra of independent samples from 38 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Bifonazole	1703041-01	2
Caelo	Bifonazole	18009702	7
Caelo	Bifonazole	18009704	3
Caelo	Bifonazole	14k10-B01-312067	1
Euro OTC	Bifonazole	16703-B08-333937	1
Euro OTC	Bifonazole	18041814	1
Euro OTC	Bifonazole	170304101	1
Euro OTC	Bifonazole	1206027-02	1
Euro OTC	Bifonazole	13G10N02	1
Euro OTC	Bifonazole	1703041-01	3
Euro OTC	Bifonazole	1510001-02	5
Fagron	Bifonazole	14K10-B01-306783	4
Fagron	Bifonazole	13G10-N02	2
Fagron	Bifonazole	14K10-B01-300541	6
Fagron	Bifonazole	14K10-B01-308349	2
Fagron	Bifonazole	1607-B10-324380	1
Fagron	Bifonazole	1518-B04-316619	1
Fagron	Bifonazole	16J03-B08-327046	2
Fagron	Bifonazole	16J03-B08-331029	2
Fagron	Bifonazole	18A15-B05_344514	1
Fagron	Bifonazole	16J03-B08-333937	2
Fagron	Bifonazole	18A15-B05-344515	2
Fagron	Bifonazole	18A15-B05-350644	1
Fagron	Bifonazole	18A15-B5-34716	1
Fagron	Bifonazole	18A15-B05-357781	1

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Bifonazole	18A15-B05-357230	1
Fagron	Bifonazole	11F20-N06	1
Fagron	Bifonazole	12E29-N03	5
Fagron	Bifonazole	14C28-B03-292388	1
Fagron	Bifonazole	14K10-B01-312067	2
Fagron	Bifonazole	16D07-B10-32480	1
Fagron	Bifonazole	16D07-B10-324380	1
Fagron	Bifonazole	18A15-B05-353060	1
Fagron	Bifonazole	12D17-N02	2
Fagron	Bifonazole	16J03-B08-333936	2
Fagron	Bifonazole	16D07-B10-321576	1
Fagron	Bifonazole	14K10-B01-316618	1
Fagron	Bifonazole	18A15-B05	1
Fargon	Bifonazole	14k10-b01-300541	1
Gehe	Bifonazole	15152703	1
Caelo	Bifonazole	15152701	5
Euro OTC	Bifonazole	1206027-01	2
Fagron	Bifonazole	12G11-N09	2
Fagron	Bifonazole	16D07-B10-324381	1

- 111 161 spectra from 742 *Apo-Ident* customers from a total of 31 848 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Bifonazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bifonazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	180	0	118 962
Type C	0	83	3	111 161

The substance/substance group *Bifonazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.6667 %)
Type C	100.0000 % (> 99.8899 %)	96.5116 % (> 93.0233 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bifonazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clotrimazole	27.01	—
Midazolam hydrochloride	40.29	—
Ciprofloxacin hydrochloride	51.51	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bifonazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20820	23364	2.56	38.91
20810	20810	0.00	38.26
21631	20810	2.90	40.88
22253	22253	0.00	39.61
22906	22253	5.69	38.33
22907	20810	2.77	38.95
22941	23364	1.50	39.08
22955	23364	1.60	39.04
23364	23364	0.00	39.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Biotin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20414-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Biotin; Biotinum

Special notes

When selecting the *Biotin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Biotin	7	7	27

Second-stage model

For differentiation of the substance/substance group *Biotin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Biotin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Biotin	16164313	22901	40	20160616
Caelo	Biotin	16164313	22902	40	20160216
Caelo	Biotin	163432	23029	40	20170119*
Caelo	Biotin	163432	23063	40	20170119*
Euro OTC	Biotin	1402028-01	21632	60	20140404
Euro OTC	Biotin	1508030	21904	60	20150925*
Euro OTC	Biotin	1610003	22855	40	20161110*
Fagron	Biotin	13K29-N02	21221	40	20131204
Fagron	Biotin	17K20-B03-351524	24694	40	20180108

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 9 reference samples from the substance/substance group *Biotin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 289 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Biotin*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Biotin	173152	23829	40
Caelo	Biotin	183009	24372	40
Euro OTC	Biotin	1603017	22507	40
Euro OTC	Biotin	1708007	23728	40
Euro OTC	Biotin	1802022	23955	40
Euro OTC	Biotin	1903020	24612	40
Euro OTC	Biotin	1903019	24631	40

- 118 862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 48 spectra from 21 *Apo-Ident* customers from 30 batches from the substance/substance group *Biotin*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Biotin	1402028-01	2
Caelo	Biotin	12A23-N03	1
EuRho	Biotin	1802022-01	1
Euro OTC	Biotin	2041517	1
Euro OTC	Biotin	3021501	1
Euro OTC	Biotin	1603017-01	1
Euro OTC	Biotin	1610003-01	5
Euro OTC	Biotin	1708007-01	3
Euro OTC	Biotin	24011801	1
Euro OTC	Biotin	161000301	1
Euro OTC	Biotin	1802022-01	4
Euro OTC	Biotin	5121812	1
Euro OTC	Biotin	28071506	1
Euro OTC	Biotin	1411047-01	1
Euro OTC	Biotin	170800701	1
Euro OTC	Biotin	1301026-01	3
Euro OTC	Biotin	1903019-01	2
Fagron	Biotin	13081203	1
Fagron	Biotin	13111202	1
Fagron	Biotin	12111302	1
Fagron	Biotin	14d04-b07-292963	1
Fagron	Biotin	12C14-N01	1
Fagron	Biotin	12A23-N03	1
Fagron	Biotin	20110634	1
Gatt-Koller	Biotin	1634211	1
Euro OTC	Biotin	1111039-02	1
kögl	Biotin	17315206	1
KÖGL	Biotin	17315212	1
Euro OTC	Biotin	10061709	1
privat	Biotin	20171208-05-100	1
Euro OTC	Biotin	1402028-01	2
Fagron	Biotin	17K20-B03-351524	1
Fagron	Biotin	13K29-N02	2

- 111 199 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Biotin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Biotin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	280	0	118 862
Type C	0	48	0	111 199

The substance/substance group *Biotin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 87.5000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Biotin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Softisan [®] 601	55.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Biotin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21221	21904	6.89	55.62
21632	21904	4.70	53.24
21904	21904	0.00	53.87
22855	22855	0.00	53.22
22901	21904	2.75	52.74
22902	21904	2.93	52.45
23029	23029	0.00	51.95
23063	23063	0.00	52.47
24694	23029	5.43	51.37

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Bismuth gallath, basic**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21252-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Bismuth gallath, basic; Bismuthi subgallas

Special notes

When selecting the *Bismuth gallath, basic* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Bismuth gallath, basic	5	2	164

Second-stage model

For differentiation of the substance/substance group *Bismuth gallath, basic* the following second-stage model is used:

- [Submodel 7](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Bismuth gallath, basic*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Bismuth gallath,...	13179105	21252	40	1412254
Caelo	Bismuth gallath,...	13179105	21553	60	20130701
Caelo	Bismuth gallath,...	170041	23359	40	20170214*
Caelo	Bismuth gallath,...	17004102	23372	40	20170214
Fagron	Bismuth gallath,...	15B02-B04-309481	22597	40	20150226
Fagron	Bismuth gallath,...	15J26-B02-317883	22598	40	20151102

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Bismuth gallath, basic*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Bismuth gallath, basic*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Bismuth gallath, basic	191063	24714	40
Fagron	Bismuth gallath, basic	16K17-B04-335597	23570	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 450 spectra from 221 *Apo-Ident* customers from 174 batches from the substance/substance group *Bismuth gallath, basic*.
- Among them are spectra of independent samples from 165 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Bismuth gallath, basic	15200905	1
Caelo	Bismuth gallath, basic	15200913	4
Caelo	Bismuth gallath, basic	1520913	1
ahd/lamotte	Bismuth gallath, basic	13718_b13_292058	1
Alliance	Bismuth gallath, basic	12172402	1
Alliance H.	Bismuth gallath, basic	15080602	1
Alliance Healthcare	Bismuth gallath, basic	13D19-N02	2
Allianz Healthcare	Bismuth gallath, basic	15200911	1
Anzag	Bismuth gallath, basic	2012000059	2
Apomix/Noweda	Bismuth gallath, basic	13D19-N02	1
Bombastus	Bismuth gallath, basic	13G10-N12	1
Bombastus	Bismuth gallath, basic	13/18-B13-292058	1
Caelo	Bismuth gallath, basic	92057409	1
Caelo	Bismuth gallath, basic	12166901	2
Caelo	Bismuth gallath, basic	81297468	5
Caelo	Bismuth gallath, basic	12I13-N11	1
Caelo	Bismuth gallath, basic	12C13-N03	1
Caelo	Bismuth gallath, basic	1127203	1
Caelo	Bismuth gallath, basic	8129768	1
Caelo	Bismuth gallath, basic	12172401	1
Caelo	Bismuth gallath, basic	B-150513-1	1
Caelo	Bismuth gallath, basic	1217240	1
Caelo	Bismuth gallath, basic	10D23-N05	1
Caelo	Bismuth gallath, basic	11127104	1
Caelo	Bismuth gallath, basic	23121410	1
Caelo	Bismuth gallath, basic	12172412	3
Caelo	Bismuth gallath, basic	15080602	3
Caelo	Bismuth gallath, basic	15B02-B04-309481	2
Caelo	Bismuth gallath, basic	10135109	1
Caelo	Bismuth gallath, basic	9K26-N10	2
Caelo	Bismuth gallath, basic	14224105	2

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Supplier	Substance	Batch	Spectra
Caelo	Bismuth gallath, basic	15J26_B02-321313	1
Caelo	Bismuth gallath, basic	15200910	1
Caelo	Bismuth gallath, basic	62183516	1
Caelo	Bismuth gallath, basic	15J26-B02-320479	1
Caelo	Bismuth gallath, basic	16038310	4
Caelo	Bismuth gallath, basic	16038312	6
Caelo	Bismuth gallath, basic	17-E16-B02-336992	1
Caelo	Bismuth gallath, basic	17004109	6
Caelo	Bismuth gallath, basic	17004107	4
Caelo	Bismuth gallath, basic	18A29-B06	1
Caelo	Bismuth gallath, basic	26011903	1
Caelo	Bismuth gallath, basic	19106301	1
Caelo	Bismuth gallath, basic	15J26-B02-320473	1
Caelo	Bismuth gallath, basic	9205701	1
Caelo	Bismuth gallath, basic	12c13-no3	1
Caelo	Bismuth gallath, basic	16K17-B04-335597	1
Caelo	Bismuth gallath, basic	2017002570	1
Caelo	Bismuth gallath, basic	12E16-N03	1
Caelo	Bismuth gallath, basic	15080603	1
Caelo	Bismuth gallath, basic	17004112	9
Caelo	Bismuth gallath, basic	15B02B04304413	1
Caelo	Bismuth gallath, basic	15200911	5
Caelo	Bismuth gallath, basic	12172409	6
Caelo	Bismuth gallath, basic	17E16-B02-336992	1
Caelo	Bismuth gallath, basic	17259503	1
Caelo	Bismuth gallath, basic	9205703	2
Caelo	Bismuth gallath, basic	16038308	7
Caelo	Bismuth gallath, basic	2012006724	1
Caelo	Bismuth gallath, basic	13179111	6
Caelo	Bismuth gallath, basic	2414E-01185	1
Caelo	Bismuth gallath, basic	13I18-B13-294108	1
Caelo	Bismuth gallath, basic	1725909	1
Caelo	Bismuth gallath, basic	14224103	4
Caelo	Bismuth gallath, basic	15200904	2
Caelo	Bismuth gallath, basic	5208I-01185	1
Caelo	Bismuth gallath, basic	1520910	1
Caelo	Bismuth gallath, basic	15200907	1
Caelo	Bismuth gallath, basic	18040801	3
Caelo	Bismuth gallath, basic	18A29-B06-346305	2
Caelo	Bismuth gallath, basic	17259509	3
Caelo	Bismuth gallath, basic	17259513	1
Caelo	Bismuth gallath, basic	17259510	5
Caelo	Bismuth gallath, basic	17259517	1
Caelo	Bismuth gallath, basic	13D19-N02	2
Caelo	Bismuth gallath, basic	13/18-B13-292057	1
Caelo	Bismuth gallath, basic	17004106	7
Caelo	Bismuth gallath, basic	15B02-B04-304408	1
Caelo	Bismuth gallath, basic	17259519	1
Caelo	Bismuth gallath, basic	12172402	4
Caelo	Bismuth gallath, basic	13179101	1
Caelo	Bismuth gallath, basic	13/18-B13-292058	1
Caelo	Bismuth gallath, basic	13I18-B13	1
Caelo	Bismuth gallath, basic	15080606	9
Caesar & Loretz GmbH	Bismuth gallath, basic	17004102	1
Caesar & Loretz GmbH	Bismuth gallath, basic	17259513	3
Caesar & Loretz GmbH	Bismuth gallath, basic	17259510	1
Caesar & Loretz GmbH	Bismuth gallath, basic	16038312	2
Caesar/Ebert	Bismuth gallath, basic	17259509	1
Euro OTC	Bismuth gallath, basic	16K17-B04-335597	3
Fagron	Bismuth gallath, basic	15H05-B07-311880	5

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Bismuth gallath, basic	2010002685	2
Fagron	Bismuth gallath, basic	2012000059	3
Fagron	Bismuth gallath, basic	11F15-N03	1
Fagron	Bismuth gallath, basic	12C13-N03	4
Fagron	Bismuth gallath, basic	12K26-N01	3
Fagron	Bismuth gallath, basic	12/13-N11	1
Fagron	Bismuth gallath, basic	12E16-N03	1
Fagron	Bismuth gallath, basic	2012006724	2
Fagron	Bismuth gallath, basic	411092-3-P	1
Fagron	Bismuth gallath, basic	13F10-N12	1
Fagron	Bismuth gallath, basic	13G10-N12	4
Fagron	Bismuth gallath, basic	13K08-N03	4
Fagron	Bismuth gallath, basic	13/18-B13-292058	1
Fagron	Bismuth gallath, basic	13/18-B13-292057	2
Fagron	Bismuth gallath, basic	13I18-b13-292057	1
Fagron	Bismuth gallath, basic	13i18-b13-294108	1
Fagron	Bismuth gallath, basic	13I18-B13-294108	6
Fagron	Bismuth gallath, basic	15B02-B04-304408	7
Fagron	Bismuth gallath, basic	14H13-B07-303639	6
Fagron	Bismuth gallath, basic	13I18-B13-292058	1
Fagron	Bismuth gallath, basic	1318b13292058	1
Fagron	Bismuth gallath, basic	13I18-B13	5
Fagron	Bismuth gallath, basic	12B02-B04-304408	1
Fagron	Bismuth gallath, basic	15b02b04304408	1
Fagron	Bismuth gallath, basic	2014006082	1
Fagron	Bismuth gallath, basic	15B02-B04-311878	1
Fagron	Bismuth gallath, basic	15b02-B04-309481	1
Fagron	Bismuth gallath, basic	15C27-B02-311879	1
Fagron	Bismuth gallath, basic	2013006220	1
Fagron	Bismuth gallath, basic	2015000866	1
Fagron	Bismuth gallath, basic	2015000361	2
Fagron	Bismuth gallath, basic	15J26-B02-320473	5
Fagron	Bismuth gallath, basic	2015007568	4
Fagron	Bismuth gallath, basic	15126-B02-321313	1
Fagron	Bismuth gallath, basic	15J26-B02-325472	7
Fagron	Bismuth gallath, basic	15J26-B02-325450	1
Fagron	Bismuth gallath, basic	17/26-B01-340556	3
Fagron	Bismuth gallath, basic	17i26-B01	1
Fagron	Bismuth gallath, basic	17/26-B01-341866	1
Fagron	Bismuth gallath, basic	17I26-B01-340552	3
Fagron	Bismuth gallath, basic	17I26-B01-341866	4
Fagron	Bismuth gallath, basic	18A29-B06-346303	1
Fagron	Bismuth gallath, basic	18G06-B10-353916	5
Fagron	Bismuth gallath, basic	18A29B06-346305	1
Fagron	Bismuth gallath, basic	10H31-N01	1
Fagron	Bismuth gallath, basic	15J26-B02	4
Fagron	Bismuth gallath, basic	16K17-B04	1
Fagron	Bismuth gallath, basic	13D19-N02	3
Fagron	Bismuth gallath, basic	13E21-N03	2
Fagron	Bismuth gallath, basic	13/18-B13294098	1
Fagron	Bismuth gallath, basic	13/18-B-13-292057	1
Fagron	Bismuth gallath, basic	13179111	1
Fagron	Bismuth gallath, basic	17G06-B10-355772	1
Fagron	Bismuth gallath, basic	18A29-B06-346305	1
Fagron	Bismuth gallath, basic	1318B1329409	1
Fagron	Bismuth gallath, basic	2018000237	2
Fagron	Bismuth gallath, basic	17I26-B01-340556	3
Fagron	Bismuth gallath, basic	15H05-B07	1
Fagron	Bismuth gallath, basic	325472	1
Fagron	Bismuth gallath, basic	15B02-B04-209481	1

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Supplier	Substance	Batch	Spectra
Fagron	Bismuth gallath, basic	1318-B13-292057	2
Fagron	Bismuth gallath, basic	13I18-B13-292057	1
Fagron	Bismuth gallath, basic	13I18-B13-294098	4
Fagron	Bismuth gallath, basic	13/18-B13-294098	2
Fagron	Bismuth gallath, basic	15J26-B022	1
Fagron	Bismuth gallath, basic	15J26-B02-321313	5
Fagron	Bismuth gallath, basic	16K17B04335597	2
Fagron	Bismuth gallath, basic	2016006984	1
Fagron	Bismuth gallath, basic	5121	1
Fagron	Bismuth gallath, basic	14H13-B07	1
Fagron	Bismuth gallath, basic	15J26-B02-321313	2
Fagron	Bismuth gallath, basic	180307BB/2016006984	1
Fagron	Bismuth gallath, basic	180808186	1
Fagron	Bismuth gallath, basic	1726B01341866	1
Fagron	Bismuth gallath, basic	1318B13294108	1
Fagron	Bismuth gallath, basic	15B02B04309481	1
Fagron	Bismuth gallath, basic	16K17B04	1
Fagron	Bismuth gallath, basic	18A29-B06-346305	3
Fagron	Bismuth gallath, basic	14H13B07303639	1
Fagron	Bismuth gallath, basic	15B02-B04-304413	5
Fagron	Bismuth gallath, basic	2017006945	3
Fagron	Bismuth gallath, basic	19B05-B09-191022	1
Fagron	Bismuth gallath, basic	13/18-B13-294108	3
Fagron	Bismuth gallath, basic	15B02-B04	2
Fagron	Bismuth gallath, basic	16K17-B04-335597	8
Fagron	Bismuth gallath, basic	17E16-B02	3
Fagron	Bismuth gallath, basic	18A29-B06-3460303	1
Fagron	Bismuth gallath, basic	18G06-B10-352463	2
Fagron	Bismuth gallath, basic	2018005145	2
Fagron	Bismuth gallath, basic	18G06-B10-355772	1
Fagron	Bismuth gallath, basic	18G06-B10-352486	2
Fagron	Bismuth gallath, basic	18G06-B10-353902	1
Fargon	Bismuth gallath, basic	13/18-B13-294108	1
Fargon GmbH & Co.KG	Bismuth gallath, basic	15J26-B02-321313	2
Fargon/ Noweda	Bismuth gallath, basic	15B02-B04-309481	1
Fargron	Bismuth gallath, basic	13D19-N02	1
Frago/Noweda	Bismuth gallath, basic	16K17-B04-335597	1
Fragon	Bismuth gallath, basic	19B05-B09-191022	1
Fragon/Sanacorp	Bismuth gallath, basic	16K17-B04-335593	1
Fragon/Sanacorp	Bismuth gallath, basic	17/26-B01-340552	1
Fragon/Sanacorp	Bismuth gallath, basic	18A-29-B06-346303	1
Gehe	Bismuth gallath, basic	12172401	1
GEHE	Bismuth gallath, basic	18A29-B06	2
GEHE	Bismuth gallath, basic	18040801	1
GEHE	Bismuth gallath, basic	17259509	1
Fagron	Bismuth gallath, basic	15/26-B02-320473	1
Caelo	Bismuth gallath, basic	12c13-n03	1
Hedinger	Bismuth gallath, basic	16038310	1
Infectopharm	Bismuth gallath, basic	14224103	1
Kehr	Bismuth gallath, basic	17I26-B01-341866	1
Klenk	Bismuth gallath, basic	12E16-N03	1
L12	Bismuth gallath, basic	16038308	1
Martinus Apotheke	Bismuth gallath, basic	keine	1
Phoenix	Bismuth gallath, basic	1520913	1
PHOENIX am 17.01.2014	Bismuth gallath, basic	2012006724	1
Phoenix, Jembke	Bismuth gallath, basic	10135101	1
phönix	Bismuth gallath, basic	15J26-B02-325450	1
Phönix	Bismuth gallath, basic	12-13-N11	1
Phönix	Bismuth gallath, basic	12E16-N03	1
Fagron	Bismuth gallath, basic	16K17-B04-335593	1

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Supplier	Substance	Batch	Spectra
Caelo	Bismuth gallath, basic	17/26-B01-340556	1
sanacorp	Bismuth gallath, basic	13/1818B13-292057	1
Sanacorp	Bismuth gallath, basic	12/13-N11	1
Sanacorp	Bismuth gallath, basic	13D19-N02	1
Sidonia	Bismuth gallath, basic	15J-26-B02-325450	1
Sidonia	Bismuth gallath, basic	15200904	1
Sidonia	Bismuth gallath, basic	17004107	3
siehe WE-Prüfprotokoll	Bismuth gallath, basic	4/09	1
Caelo	Bismuth gallath, basic	17004102	8
Caelo	Bismuth gallath, basic		1
Fagron	Bismuth gallath, basic		1
Fagron	Bismuth gallath, basic	15J26-B02-317883	8
Fagron	Bismuth gallath, basic	15B02-B04-309481	2
Caelo	Bismuth gallath, basic	13179105	1

- 110 797 spectra from 742 *Apo-Ident* customers from a total of 31 718 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Bismuth gallath, basic* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bismuth gallath, basic* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	80	0	119 062
Type C	0	449	1	110 797

The substance/substance group *Bismuth gallath, basic* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	99.7778 % (> 99.1111 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Bismuth gallath, basic* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	79.50	—
⋮	⋮	⋮
Folic acid hydrate	>50	102.61
Acetylcysteine	>50	642.28

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bismuth gallath, basic* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22598	21252	2.83	104.93
23359	23359	0.00	112.26
23372	21252	2.70	107.80
21252	21252	0.00	102.72
21553	21252	3.27	105.27
22597	21252	3.10	105.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Boric acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20182-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Boric acid; Acidum boricum

Special notes

When selecting the *Boric acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Boric acid	5	2	31

Second-stage model

For differentiation of the substance/substance group *Boric acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Boric acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Boric acid	14133119	21804	60	20140509
Caelo	Boric acid	15425112	22964	40	20160104
Caelo	Boric acid	170613	23286	40	20170316*
Fagron	Boric acid	13I04-N06	21228	40	20130920
Fagron	Boric acid	15L09-B07-322988	23746	40	20151222

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Boric acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Boric acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Boric acid	15242903	22965	40
Caelo	Boric acid	191943	24741	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 51 spectra from 33 *Apo-Ident* customers from 36 batches from the substance/substance group *Boric acid*.
- Among them are spectra of independent samples from 31 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Boric acid	9324021	1
Caelo	Boric acid	9324043	1
Caelo	Boric acid	12238901	1
Caelo	Boric acid	10227913	1
Caelo	Boric acid	14133113	2
Caelo	Boric acid	15095103	2
Caelo	Boric acid	15158901	1
Caelo	Boric acid	15158903	1
Caelo	Boric acid	80303AB	1
Caelo	Boric acid	15425118	2
Caelo	Boric acid	15242906	1
Caelo	Boric acid	16291001	1
Caelo	Boric acid	15242909	1
Caelo	Boric acid	9324036	1
Caelo	Boric acid	11D13-N08	1
Caelo	Boric acid	14095202	1
Caelo	Boric acid	15425108	2
Caelo	Boric acid	15425114	2
Caelo	Boric acid	5425114	1
Caelo	Boric acid	17327907	3
Caelo	Boric acid	17327912	2
Caelo	Boric acid	15425101	5
E Plus	Boric acid	15425108	1
Fagron	Boric acid	11d13-n08	1
Fagron	Boric acid	12f01-n08	1
Fagron	Boric acid	11I26-n05	1
Fagron	Boric acid	12G04-N10	1
Fagron	Boric acid	9082012B	1
Fagron	Boric acid	14133101	1
Fagron	Boric acid	14B07-B02-295752	1
Gatt-Koller	Boric acid	1803542	1
Caelo	Boric acid	12260502	1
Sanacorp	Boric acid	1/AKD3	1
Caelo	Boric acid	14133119	1
Caelo	Boric acid	15425112	2
Fagron	Boric acid	13I04-N06	2
Nachprüfung	Boric acid		1

- 111 196 spectra from 742 *Apo-Ident* customers from a total of 31 856 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Boric acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Boric acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	51	0	111 196

The substance/substance group *Boric acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 88.2353 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Boric acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	43.39	—
Levothyroxin sodium	50.70	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Boric acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21228	23286	15.82	60.64
21804	23286	20.15	60.99
22964	23286	10.17	60.47
23286	23286	0.00	60.02
23746	23286	16.81	60.85

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Budesonide, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20569-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Budesonide, micronized; Budesonidum micronisatum

Special notes

When selecting the *Budesonide, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Budesonide, micronized	7	6	99

Second-stage model

For differentiation of the substance/substance group *Budesonide, micronized* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Budesonide, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Budesonide, micr...	11351704	20808	40	AR-15-FG-005286-01
Caelo	Budesonide, micr...	161431	22627	40	20160606*
Caelo	Budesonide, micr...	161431	22627SI	25	20160606*
Caelo	Budesonide, micr...	15344004	22649	40	20151116
Caelo	Budesonide, micr...	15344004	22649SI	23	20151116
Euro OTC	Budesonide, micr...	1311022-01	21620	60	20140113
Euro OTC	Budesonide, micr...	1311022-01	21620SI	37	20140113
Euro OTC	Budesonide, micr...	1604018	22537	40	20160509*
Euro OTC	Budesonide, micr...	1604018	22537SI	23	20160509*
Fagron	Budesonide, micr...	16J04-B01-326581	22841	40	20161026
Fagron	Budesonide, micr...	16J04-B01-326581	22888	40	20161026
Fagron	Budesonide, micr...	16J04-B01-326581	22888SI	30	20161026
Fagron	Budesonide, micr...	18C15-B03-355399	24699	40	20180409

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 478 spectra of 13 reference samples from the substance/substance group *Budesonide, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 211 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 430 spectra of 14 reference samples from the substance/substance group *Budesonide, micronized*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Budesonide, micronized	11351706	20800	40
Caelo	Budesonide, micronized	170788	23279	40
Caelo	Budesonide, micronized	180749	24026	40
Caelo	Budesonide, micronized	191381	24737	40
Euro OTC	Budesonide, micronized	1709022	23778	40
Euro OTC	Budesonide, micronized	1904004	24619	40
Caelo	Budesonide, micronized	15344004	22649SI [†]	7
Caelo	Budesonide, micronized	170788	23279SI	20
Caelo	Budesonide, micronized	180749	24026SI	20
Caelo	Budesonide, micronized	191381	24737SI	24
Euro OTC	Budesonide, micronized	1709022	23778SI	20
Euro OTC	Budesonide, micronized	1904004	24619SI	40
Fagron	Budesonide, micronized	16J04-B01-326581	22841SI [†]	24
Fagron	Budesonide, micronized	18C15-B03-355399	24699SI [†]	35

- 118 712 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 278 spectra from 107 *Apo-Ident* customers from 101 batches from the substance/substance group *Budesonide, micronized*.
- Among them are spectra of independent samples from 99 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Budesonide, micronized	21100M1A0021321	1
Caelo	Budesonide, micronized	21100M1	1
Caelo	Budesonide, micronized	12295111	5
Caelo	Budesonide, micronized	11175014	2
Caelo	Budesonide, micronized	11351707	3
Caelo	Budesonide, micronized	11351706	5
Caelo	Budesonide, micronized	11351701	1
Caelo	Budesonide, micronized	11351703	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Budesonide, micronized	11175015	1
Caelo	Budesonide, micronized	12295108	1
Caelo	Budesonide, micronized	14071702	6
Caelo	Budesonide, micronized	14071707	3
Caelo	Budesonide, micronized	14071717	3
Caelo	Budesonide, micronized	ChB14071717	1
Caelo	Budesonide, micronized	15173806	2
Caelo	Budesonide, micronized	15173811	6
Caelo	Budesonide, micronized	15044002	1
Caelo	Budesonide, micronized	15344012	3
Caelo	Budesonide, micronized	15344008	8
Caelo	Budesonide, micronized	15344013	1
Caelo	Budesonide, micronized	16143103	2
Caelo	Budesonide, micronized	16143101	4
Caelo	Budesonide, micronized	774865	1
Caelo	Budesonide, micronized	10061705	1
Caelo	Budesonide, micronized	16143108	8
Caelo	Budesonide, micronized	16143106	2
Caelo	Budesonide, micronized	170078801	1
Caelo	Budesonide, micronized	17078805	7
Caelo	Budesonide, micronized	16143112	2
Caelo	Budesonide, micronized	16143105	2
Caelo	Budesonide, micronized	17078809	4
Caelo	Budesonide, micronized	18074901	2
Caelo	Budesonide, micronized	17342902	2
Caelo	Budesonide, micronized	18172603	6
Caelo	Budesonide, micronized	18172604	9
Caelo	Budesonide, micronized	18074909	1
Caelo	Budesonide, micronized	18172608	2
Caelo	Budesonide, micronized	17078808	5
Caelo	Budesonide, micronized	12295110	4
Caelo	Budesonide, micronized	18074907	3
Caelo	Budesonide, micronized	14071714	6
Caelo	Budesonide, micronized	18172601	1
Caelo	Budesonide, micronized	18074908	2
Caelo	Budesonide, micronized	17078801	10
Caelo	Budesonide, micronized	11351713	1
Caelo	Budesonide, micronized	12295105	1
Caelo	Budesonide, micronized	19138103	1
Caelo	Budesonide, micronized	12295106	2
Caelo	Budesonide, micronized	14071701	2
Caelo	Budesonide, micronized	15344003	7
Caelo	Budesonide, micronized	15344006	1
Caelo	Budesonide, micronized	15344005	3
Caelo	Budesonide, micronized	18074902	7
Caelo	Budesonide, micronized	18172611	2
Caelo	Budesonide, micronized	18172610	1
Caelo	Budesonide, micronized	19138102	1
Caelo	Budesonide, micronized	12295103	1
Caelo	Budesonide, micronized	15173803	5
Caelo	Budesonide, micronized	15173802	4
Caelo	Budesonide, micronized	15173810	1
Caelo	Budesonide, micronized	15344002	2
Caelo	Budesonide, micronized	15344014	1
Caelo	Budesonide, micronized	17078803	2
Caelo	Budesonide, micronized	18074903	3
Fagron	Budesonide, micronized	18074901	1
Fagron	Budesonide, micronized	18172601	1
Caelo	Budesonide, micronized	14071713	1
Caelo	Budesonide, micronized	15344010	3

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Supplier	Substance	Batch	Spectra
Caelo	Budesonide, micronized	17078804	4
Caelo	Budesonide, micronized	12295109	2
Caelo	Budesonide, micronized	14071716	2
Caelo	Budesonide, micronized	16143107	3
Caelo	Budesonide, micronized	18074905	4
Caelo	Budesonide, micronized	140711707	1
Caelo	Budesonide, micronized	1471707	1
Caelo	Budesonide, micronized	15173807	3
Caesolo ,	Budesonide, micronized	17078809	1
Caesar & Loretz GmbH	Budesonide, micronized	17342902	1
Caesar & Loretz GmbH	Budesonide, micronized	18074905	1
Caesar & Loretz GmbH	Budesonide, micronized	18172610	1
Caesar & Loretz GmbH	Budesonide, micronized	19138103	1
Caesar & Loretz GmbH	Budesonide, micronized	18172608	1
Caesar & Loretz GmbH/Ph...	Budesonide, micronized	18172606	1
Cealo	Budesonide, micronized	17078804	1
crystal pharma/gehe	Budesonide, micronized	1305004-01	2
Euro OTC	Budesonide, micronized	1604018-01	1
Fagron	Budesonide, micronized	12G23-N01	2
Fagron	Budesonide, micronized	13A07-N09	1
Fagron	Budesonide, micronized	13H22-N03	2
Fagron	Budesonide, micronized	14H15-B02	3
Fagron	Budesonide, micronized	14H15-B02-297926	1
Fagron	Budesonide, micronized	15E27-B10-308321	1
Fagron	Budesonide, micronized	14H15-B02-301971	2
Fagron	Budesonide, micronized	15E27-B01-308321	1
Fagron	Budesonide, micronized	17A17-B01-331248	1
Fagron	Budesonide, micronized	15E27-B10-315704	1
Fagron	Budesonide, micronized	17F28-B04-345016	1
Fagron	Budesonide, micronized	15344012	1
Fagron	Budesonide, micronized	17A17-B01-331448	1
Fagron	Budesonide, micronized	14A30-B09-291366	2
Fagron	Budesonide, micronized	14H15-B02-301972	1
Fagron	Budesonide, micronized	15E27_B10	1
Fagron	Budesonide, micronized	15E27-B10-308322	1
Fargon/Kehr	Budesonide, micronized	16J04-B01-326583	1
GEHE	Budesonide, micronized	18074901	1
GEHE	Budesonide, micronized	18172601	2
Caelo	Budesonide, micronized	15344009	1
L10	Budesonide, micronized	15344012	1
Noweda	Budesonide, micronized	16143108	1
Noweda	Budesonide, micronized	16143110	1
Noweda	Budesonide, micronized	1604018-01	1
Noweda	Budesonide, micronized	17078803	1
Caelo	Budesonide, micronized	14071706	1
Caelo	Budesonide, micronized	16143102	2
phoenix	Budesonide, micronized	19138103	1
Phoenix	Budesonide, micronized	14071702	3
Phoenix	Budesonide, micronized	15344013	1
Fagron	Budesonide, micronized	14A30-B09_291366	1
sanacorp	Budesonide, micronized	14071701	1
Sanacorp,	Budesonide, micronized	16143103	1
VDI 23.10.14 19,50 euro	Budesonide, micronized	14071707	1
Caelo	Budesonide, micronized	15344004	1
Euro OTC	Budesonide, micronized	1311022-01	5

- 110 969 spectra from 742 *Apo-Ident* customers from a total of 31 792 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are docu-

mented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Budesonide, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Budesonide, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	478	0	110 211
Type B	0	430	0	118 712
Type C	0	274	4	110 969

The substance/substance group *Budesonide, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7448 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.6047 %)
Type C	100.0000 % (> 99.8899 %)	98.5612 % (> 97.4820 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Budesonide, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol valerate	22.18	—
Dexamethasone	34.91	61.13
Ciclosporin	38.11	—
Prednisolon dihydrogen phosphate dinat...	43.14	—
Erythromycin	45.22	36.35
Fusidic acid	51.74	—
⋮	⋮	⋮
Betamethasone valerate	>50	41.25
Prednicarbate, micronized	>50	52.39
Triamcinolone acetonide	>50	58.58
Prednisolone, micronized	>50	82.02
Triamcinolone, micronized	>50	181.37
Capsaicin	>50	200.96
Prednisone	>50	208.79

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Substanz	Distance in main model	Distance in second-stage model
Heparin sodium	>50	208.90
Betamethasone, micronized	>50	225.42
Norethisterone acetate	>50	227.24

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Budesonide, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22888	22627	2.79	34.51
21620	20808	4.57	40.23
22537	22537	0.00	34.88
24699	22627	3.48	35.22
20808	20808	0.00	41.95
22627	22627	0.00	34.86
22841	22627	1.19	34.81
22649	22627	3.74	34.20

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Butylated hydroxytoluene**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21307-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Butylated hydroxytoluene; Butylhydroxytoluenum

Special notes

When selecting the *Butylated hydroxytoluene* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Butylated hydroxytoluene	4	2	59

Second-stage model

For differentiation of the substance/substance group *Butylated hydroxytoluene* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Butylated hydroxytoluene*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Butylated hydrox...	13354602	21307	40	20131105
Caelo	Butylated hydrox...	13354604	21355	40	AR-15-FG-007846-02
Caelo	Butylated hydrox...	15172103	21911	60	20150529
Caelo	Butylated hydrox...	15172103	22281	60	20150529
Caelo	Butylated hydrox...	15172103	22350	60	20150529
Caelo	Butylated hydrox...	190749	24554	40	20190405*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *Butylated hydroxytoluene*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 389 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Butylated hydroxytoluene*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Butylated hydroxytoluene	163163	23356	40
Caelo	Butylated hydroxytoluene	180291	24019	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 350 spectra from 240 *Apo-Ident* customers from 62 batches from the substance/substance group *Butylated hydroxytoluene*.
- Among them are spectra of independent samples from 59 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Butylated hydroxytoluene	18029102	1
Caelo	Butylated hydroxytoluene	12382304	7
Caelo	Butylated hydroxytoluene	122080206	1
Apo Ident/ Noweda	Butylated hydroxytoluene	18029104	1
Bombastus	Butylated hydroxytoluene	13354604	1
Caelo	Butylated hydroxytoluene	20161112-1	1
Caelo	Butylated hydroxytoluene	12207005	3
Caelo	Butylated hydroxytoluene	2113U02851	1
Caelo	Butylated hydroxytoluene	12382302	5
Caelo	Butylated hydroxytoluene	12382307	1
Caelo	Butylated hydroxytoluene	12382309	8
Caelo	Butylated hydroxytoluene	7031403	1
Caelo	Butylated hydroxytoluene	12382312	1
Caelo	Butylated hydroxytoluene	13354611	4
Caelo	Butylated hydroxytoluene	14300501	10
Caelo	Butylated hydroxytoluene	1400501	1
Caelo	Butylated hydroxytoluene	13354609	2
Caelo	Butylated hydroxytoluene	14300505	6
Caelo	Butylated hydroxytoluene	2749	1
Caelo	Butylated hydroxytoluene	14300503	2
Caelo	Butylated hydroxytoluene	231115BHT	1
Caelo	Butylated hydroxytoluene	1426801	1
Caelo	Butylated hydroxytoluene	716M-02851	1
Caelo	Butylated hydroxytoluene	16316301	14
Caelo	Butylated hydroxytoluene	2170717	1
Caelo	Butylated hydroxytoluene	16316305	9
Caelo	Butylated hydroxytoluene	163163055402	1
Caelo	Butylated hydroxytoluene	18029102	11
Caelo	Butylated hydroxytoluene	18229102	1
Caelo	Butylated hydroxytoluene	18029107	12
Caelo	Butylated hydroxytoluene	15172105	10
Caelo	Butylated hydroxytoluene	16316304	15
Caelo	Butylated hydroxytoluene	11131006	1
Caelo	Butylated hydroxytoluene	123823	1
Caelo	Butylated hydroxytoluene	11(18029107)	1
Caelo	Butylated hydroxytoluene	143004502	1

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Supplier	Substance	Batch	Spectra
Caelo	Butylated hydroxytoluene	14300502	7
Caelo	Butylated hydroxytoluene	19074902	3
Caelo	Butylated hydroxytoluene	12280203	5
Caelo	Butylated hydroxytoluene	15094501	8
Caelo	Butylated hydroxytoluene	14300506	1
Caelo	Butylated hydroxytoluene	16316304-20180619Ma5	1
Caelo	Butylated hydroxytoluene	16316307	21
Caelo	Butylated hydroxytoluene	15172101	10
Caelo	Butylated hydroxytoluene	18029104	4
Caelo	Butylated hydroxytoluene	18029105	20
Caelo	Butylated hydroxytoluene	12280206	4
Caelo	Butylated hydroxytoluene	15426807	12
Caelo	Butylated hydroxytoluene	18048701	14
Caelo	Butylated hydroxytoluene	18029108	3
Caelo	Butylated hydroxytoluene	19074901	3
Caelo	Butylated hydroxytoluene	12158201	3
Caelo	Butylated hydroxytoluene	12158204	5
Caelo	Butylated hydroxytoluene	1220705	1
Caelo	Butylated hydroxytoluene	5426807	1
Caesar & Loretz	Butylated hydroxytoluene	15426801	1
Caesar & Loretz GmbH	Butylated hydroxytoluene	18029105	3
Caesar & Loretz GmbH	Butylated hydroxytoluene	18029107	1
Caesar & Loretz GmbH	Butylated hydroxytoluene	18029108	1
Caesar & Loretz GmbH	Butylated hydroxytoluene	18029102	1
Caesar & Loretz GmbH	Butylated hydroxytoluene	19074902	2
Caesar & Loretz GmbH	Butylated hydroxytoluene	19074901	1
Caesar & Loretz GmbH/ P...	Butylated hydroxytoluene	18029107	1
Celo	Butylated hydroxytoluene	15426801	1
Fagron	Butylated hydroxytoluene	15426801	1
Fagron	Butylated hydroxytoluene	16316304	1
Fagron	Butylated hydroxytoluene	11308701	1
Fiebig	Butylated hydroxytoluene	15426807	1
Fiebig	Butylated hydroxytoluene	18029105	1
Gehe	Butylated hydroxytoluene	15426807	1
Gehe	Butylated hydroxytoluene	18029107	1
Gehe	Butylated hydroxytoluene	18029105	2
GEHE	Butylated hydroxytoluene	18029105	1
Caelo	Butylated hydroxytoluene	1631301	1
L12	Butylated hydroxytoluene	15426807	1
L12	Butylated hydroxytoluene	16316307	1
Nachprüfung	Butylated hydroxytoluene	123456	1
Noweda	Butylated hydroxytoluene	12158201	1
Noweda	Butylated hydroxytoluene	12382304	1
Noweda	Butylated hydroxytoluene	15172103	1
Noweda	Butylated hydroxytoluene	15426807	1
Noweda	Butylated hydroxytoluene	16316305	1
Noweda	Butylated hydroxytoluene	18029105	1
Caelo	Butylated hydroxytoluene	12280201	1
Phoenix	Butylated hydroxytoluene	3111201	1
Phoenix	Butylated hydroxytoluene	12382305	1
Phoenix	Butylated hydroxytoluene	13354609	1
Phoenix	Butylated hydroxytoluene	15426801	1
Phoenix	Butylated hydroxytoluene	16316301	1
Phönix	Butylated hydroxytoluene	16316307	1
Phönix	Butylated hydroxytoluene	18029102	1
PHÖNIX	Butylated hydroxytoluene	16316304	1
sanacorp	Butylated hydroxytoluene	15172103	1
Sanacorp	Butylated hydroxytoluene	14300505	1
Sanacorp	Butylated hydroxytoluene	16316305	1
Caelo	Butylated hydroxytoluene	15426801	9

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Supplier	Substance	Batch	Spectra
SanacorpWE:04.01.18 E...	Butylated hydroxytoluene	16316304	1
Caelo	Butylated hydroxytoluene	15172103	19
Caelo	Butylated hydroxytoluene	13354602	4
Caelo	Butylated hydroxytoluene	13354604	8

- 110 897 spectra from 742 *Apo-Ident* customers from a total of 31 831 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Butylated hydroxytoluene* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Butylated hydroxytoluene* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	80	0	119 062
Type C	0	340	10	110 897

The substance/substance group *Butylated hydroxytoluene* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	97.1429 % (> 96.2857 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Butylated hydroxytoluene* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxybuprocaine hydrochloride	50.03	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Butylated hydroxytoluene* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21307	21355	2.74	65.11
21355	21355	0.00	65.31
21911	21355	2.66	62.63
22281	21355	2.22	64.86
22350	21355	1.54	63.09
24554	24554	0.00	69.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Caffeine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20962-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Caffeine; Coffeinum

Special notes

When selecting the *Caffeine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Caffeine	6	5	64

Second-stage model

For differentiation of the substance/substance group *Caffeine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Caffeine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Caffeine	12317911	21089	40	20121113
Caelo	Caffeine	12317911	21205	40	20121113
Caelo	Caffeine	13233105	21456	60	20131008
Caelo	Caffeine	13233104	21548	60	20131008
Euro OTC	Caffeine	1211012-01	20962	40	1412248
Euro OTC	Caffeine	1808017	24199	40	20180905*
Euro OTC	Caffeine	1909022	24980	40	20191022*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Caffeine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 369 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Caffeine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Caffeine	15082303	22823	40
Euro OTC	Caffeine	1603009	22517	40
Euro OTC	Caffeine	1703006	23140	40
Euro OTC	Caffeine	1907006	24784	40
Euro OTC	Caffeine	2001041	25079	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 200 spectra from 118 *Apo-Ident* customers from 67 batches from the substance/substance group *Caffeine*.
- Among them are spectra of independent samples from 64 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Caffeine	KNC1294J14	2
Caelo	Caffeine	12317909	7
Bombastus	Caffeine	1307049-01	1
Caelo	Caffeine	11076807	2
Caelo	Caffeine	12093410	2
Caelo	Caffeine	12317904	2
Caelo	Caffeine	12317902	1
Caelo	Caffeine	12093418	2
Caelo	Caffeine	12317914	2
Caelo	Caffeine	13233111	5
Caelo	Caffeine	15054704	2
Caelo	Caffeine	15054709	3
Caelo	Caffeine	15082311	1
Caelo	Caffeine	12093402	2
Caelo	Caffeine	1503020-01	2
Caelo	Caffeine	15375007	4
Caelo	Caffeine	15082315	1
Caelo	Caffeine	17173704	7
Caelo	Caffeine	17133704	1
Caelo	Caffeine	18011901	5
Caelo	Caffeine	1703006-01	3
Caelo	Caffeine	18011902	3
Caelo	Caffeine	18011906	8
Caelo	Caffeine	1808017-01	1
Caelo	Caffeine	11111111	1
Caelo	Caffeine	18011920	5
Caelo	Caffeine	3212E-01281	1
Caelo	Caffeine	15375006	2

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Supplier	Substance	Batch	Spectra
Caelo	Caffeine	18011911	11
Caelo	Caffeine	18011915	5
Caelo	Caffeine	18077906	1
Caelo	Caffeine	9301807	1
Caelo	Caffeine	12317906	1
Caelo	Caffeine	15375012	5
Caelo	Caffeine	17173707	3
Caelo	Caffeine	15372012	1
Caelo	Caffeine	18011928	1
Caesar & Loretz GmbH	Caffeine	18011912	1
EuRho	Caffeine	17030006-02	2
Euro OTC	Caffeine	26081406	1
Euro OTC	Caffeine	180881701	1
Euro OTC	Caffeine	1603009/01	1
Euro OTC	Caffeine	1503020-01	6
Euro OTC	Caffeine	1503020-02	8
Euro OTC	Caffeine	1603009-01	2
Euro OTC	Caffeine	291001903	2
Euro OTC	Caffeine	1603009-02	3
Euro OTC	Caffeine	31071701	1
Euro OTC	Caffeine	1703006-02	3
Euro OTC	Caffeine	5101701	1
Euro OTC	Caffeine	1109017-01	1
Euro OTC	Caffeine	18808017-01	1
Euro OTC	Caffeine	1307049-01	4
Euro OTC	Caffeine	1808017-01	3
Euro OTC	Caffeine	160300901	2
Euro OTC	Caffeine	1211012-02	1
EUro/AHD	Caffeine	121012-01	1
EUro/AHD	Caffeine	1307049-01	1
Euro/Noweda	Caffeine	1703006-01	1
Euro OTC	Caffeine	1411015-01	4
Euro OTC	Caffeine	325241AX20	1
Euro OTC	Caffeine	1703006-01	19
Euro OTC	Caffeine	1808017-02	2
Fagron	Caffeine	15H11-B02	1
Gatt-Koller	Caffeine	1803747	1
Gatt-Koller / Phoenix	Caffeine	5898/12135213	2
Gehe	Caffeine	18011915	2
Merck	Caffeine	MerckReagenziensatz	1
Noweda	Caffeine	1404026-01	1
Caelo	Caffeine	1211012-01	1
Phoenix	Caffeine	1808017-01	1
Phönix	Caffeine	1603009-02	1
Euro OTC	Caffeine	16462119	1
Caelo	Caffeine	17173705	2
Caelo	Caffeine	13233105	4
Euro OTC	Caffeine	1211012-01	1
Reagenz	Caffeine		1

- 111 047 spectra from 742 *Apo-Ident* customers from a total of 31 826 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Caffeine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Caffeine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	200	0	118 942
Type C	0	198	2	111 047

The substance/substance group *Caffeine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.0000 % (> 97.5000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Caffeine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	48.81	—
Phenazone	60.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Caffeine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20962	20962	0.00	56.20
21205	24199	2.36	54.20
21456	24199	4.28	54.98
21548	24199	6.15	58.65
24199	24199	0.00	54.96
24980	24980	0.00	54.18
21089	24199	2.82	54.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Calcium ascorbate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20393-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Calcium ascorbate; Calcii ascorbinicum

Special notes

When selecting the *Calcium ascorbate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium ascorbate	7	6	11

Second-stage model

For differentiation of the substance/substance group *Calcium ascorbate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium ascorbate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium ascorbate	13105624	21313	40	20130620
Caelo	Calcium ascorbate	163111	23060	40	20161207*
Caelo	Calcium ascorbate	16311101	23518	40	20161207
Euro OTC	Calcium ascorbate	1612003	22916	40	20170110*
Euro OTC	Calcium ascorbate	1709005	23609	40	20170914*
Euro OTC	Calcium ascorbate	1709004	23611	40	20170914*
Euro OTC	Calcium ascorbate	1801010	23884	40	20180115*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Calcium ascorbate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 409 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Calcium ascorbate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium ascorbate	183226	24373	40
Euro OTC	Calcium ascorbate	1607033-01	22812	40
Euro OTC	Calcium ascorbate	1807032	24194	40
Euro OTC	Calcium ascorbate	1901003	24470	40
Euro OTC	Calcium ascorbate	1904010	24626	40
Euro OTC	Calcium ascorbate	1910003	24979	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 9 *Apo-Ident* customers from 13 batches from the substance/substance group *Calcium ascorbate*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Arktis	Calcium ascorbate	7339/4617	1
Arktis	Calcium ascorbate	733P/1518	1
Burton Feingold	Calcium ascorbate	L008415	1
Caelo	Calcium ascorbate	13105608	1
Caelo	Calcium ascorbate	14340907	1
Caelo	Calcium ascorbate	15324708	1
Caelo	Calcium ascorbate	15324702	1
Caelo	Calcium ascorbate	16311105	1
Euro OTC	Calcium ascorbate	1709004-01	1
Farmalabor / Farmalabor	Calcium ascorbate	P1104931-000A	1
Gatt-Koller	Calcium ascorbate	1900123	1
Euro OTC	Calcium ascorbate	1801010	1
Euro OTC	Calcium ascorbate	1709005	1

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium ascorbate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose,

all relevant spectra of the various substances were compared with *Calcium ascorbate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	240	0	118 902
Type C	0	13	0	111 234

The substance/substance group *Calcium ascorbate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium ascorbate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	34.55	—
Calcium citrate tetrahydrate	40.73	—
Calcium lactate pentahydrate	47.27	—
Levothyroxin sodium	49.79	—
Magnesium citrate	53.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium ascorbate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21313	22916	6.54	37.36
22916	22916	0.00	37.08
23060	23060	0.00	36.65
23518	23060	2.58	35.41
23609	23609	0.00	37.36
23611	23611	0.00	37.36
23884	23884	0.00	31.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Calcium citrate tetrahydrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20013-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Calcium citrate tetrahydrate; Calcii citras tetrahydricus

Special notes

When selecting the *Calcium citrate tetrahydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium citrate tetrahydrate	6	6	94

Second-stage model

For differentiation of the substance/substance group *Calcium citrate tetrahydrate* the following second-stage model is used:

- [Submodel 4](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium citrate tetrahydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium citrate ...	13391203	21320	40	20131205
Caelo	Calcium citrate ...	13391203	21486	40	20131205
Caelo	Calcium citrate ...	171768	23651	40	20170713*
Euro OTC	Calcium citrate ...	1305018-01	21249	40	20130528
Euro OTC	Calcium citrate ...	1509039	21931	60	20151013*
Euro OTC	Calcium citrate ...	1509039-01	22255	60	20151013
Euro OTC	Calcium citrate ...	1701001	22995	40	20170124*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Calcium citrate tetrahydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 369 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Calcium citrate tetrahydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium citrate tetrahydrate	181608	24230	40
Euro OTC	Calcium citrate tetrahydrate	1606001	22681	40
Euro OTC	Calcium citrate tetrahydrate	1707025	23606	40
Euro OTC	Calcium citrate tetrahydrate	1803031	24077	40
Euro OTC	Calcium citrate tetrahydrate	1901002	24514	40
Euro OTC	Calcium citrate tetrahydrate	1912013	25075	40

- 118902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 200 spectra from 93 *Apo-Ident* customers from 100 batches from the substance/substance group *Calcium citrate tetrahydrate*.
- Among them are spectra of independent samples from 94 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Calcium citrate tetrahydrate	11349313	2
ACM	Calcium citrate tetrahydrate	KNC0740J15	1
Alliance Health 23.10.2...	Calcium citrate tetrahydrate	1402003-01	1
Caelo	Calcium citrate tetrahydrate	11349325	2
Caelo	Calcium citrate tetrahydrate	11168813	1
Caelo	Calcium citrate tetrahydrate	11349304	2
Caelo	Calcium citrate tetrahydrate	11349309	2
Caelo	Calcium citrate tetrahydrate	11349301	1
Caelo	Calcium citrate tetrahydrate	11349318	3
Caelo	Calcium citrate tetrahydrate	11349320	1
Caelo	Calcium citrate tetrahydrate	1168813	1
Caelo	Calcium citrate tetrahydrate	19061315	1
Caelo	Calcium citrate tetrahydrate	71356168	1
Caelo	Calcium citrate tetrahydrate	12310406	5
Caelo	Calcium citrate tetrahydrate	12310411	2
Caelo	Calcium citrate tetrahydrate	12310413	4
Caelo	Calcium citrate tetrahydrate	11061402	1
Caelo	Calcium citrate tetrahydrate	16021502	1
Caelo	Calcium citrate tetrahydrate	92192429	1
Caelo	Calcium citrate tetrahydrate	15177702	2
Caelo	Calcium citrate tetrahydrate	15375707	1
Caelo	Calcium citrate tetrahydrate	15375713	6
Caelo	Calcium citrate tetrahydrate	16056501	1
Caelo	Calcium citrate tetrahydrate	1509039-02	1
Caelo	Calcium citrate tetrahydrate	1606001-02	1
Caelo	Calcium citrate tetrahydrate	1600565	1
Caelo	Calcium citrate tetrahydrate	1716803	1

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Supplier	Substance	Batch	Spectra
Caelo	Calcium citrate tetrahydrate	17176806	2
Caelo	Calcium citrate tetrahydrate	17176805	1
Caelo	Calcium citrate tetrahydrate	18160802	3
Caelo	Calcium citrate tetrahydrate	19010002-01	1
Caelo	Calcium citrate tetrahydrate	12310418	2
Caelo	Calcium citrate tetrahydrate	17176803	6
Caelo	Calcium citrate tetrahydrate	2114M1209	1
Caelo	Calcium citrate tetrahydrate	1509039-01	1
Caelo	Calcium citrate tetrahydrate	14133310	1
Caelo	Calcium citrate tetrahydrate	16056505	2
Caelo	Calcium citrate tetrahydrate	17176812	2
Caelo	Calcium citrate tetrahydrate	18160805	1
Caelo	Calcium citrate tetrahydrate	18160813	1
Caelo	Calcium citrate tetrahydrate	15177703	7
Caelo	Calcium citrate tetrahydrate	3512U-01209	1
Caelo	Calcium citrate tetrahydrate	15177701	1
Caelo	Calcium citrate tetrahydrate	133912042x	1
Caelo	Calcium citrate tetrahydrate	12310407	2
Caelo	Calcium citrate tetrahydrate	14133303	1
Caelo	Calcium citrate tetrahydrate	17176818	1
Caelo	Calcium citrate tetrahydrate	11168803	1
Caelo	Calcium citrate tetrahydrate	12310402	2
Caelo	Calcium citrate tetrahydrate	12310403	3
Caelo	Calcium citrate tetrahydrate	13391205	5
Caelo	Calcium citrate tetrahydrate	1408017-01	1
Caelo	Calcium citrate tetrahydrate	1168806	1
Caelo	Calcium citrate tetrahydrate	11168806	3
Caelo	Calcium citrate tetrahydrate	17176808	6
Caelo	Calcium citrate tetrahydrate	18160803	1
Caelo	Calcium citrate tetrahydrate	92457399	1
Caelo	Calcium citrate tetrahydrate	14133307	1
Caelo	Calcium citrate tetrahydrate	15375702	6
Caelo	Calcium citrate tetrahydrate	15375712	2
Caelo	Calcium citrate tetrahydrate	15375703	1
Caelo	Calcium citrate tetrahydrate	16056504	4
Caelo	Calcium citrate tetrahydrate	12310401	1
Caesar & Loretz GmbH	Calcium citrate tetrahydrate	18160804	1
Caelo	Calcium citrate tetrahydrate	12310401	1
Caelo	Calcium citrate tetrahydrate	12310417	3
Dr.Lohmann	Calcium citrate tetrahydrate	3042527	1
EuRho	Calcium citrate tetrahydrate	1502012-02	1
EuRho/Jenne	Calcium citrate tetrahydrate	1211007-01	1
Euro OTC	Calcium citrate tetrahydrate	1207006-01	3
Euro OTC	Calcium citrate tetrahydrate	1211007-01	2
Euro OTC	Calcium citrate tetrahydrate	13031204	1
Euro OTC	Calcium citrate tetrahydrate	3006222	1
Euro OTC	Calcium citrate tetrahydrate	1509039-02	6
Euro OTC	Calcium citrate tetrahydrate	15177704	1
Euro OTC	Calcium citrate tetrahydrate	1606001-01	1
Euro OTC	Calcium citrate tetrahydrate	1606001-02	2
Euro OTC	Calcium citrate tetrahydrate	1402003-01	2
Euro OTC	Calcium citrate tetrahydrate	1901002-01	1
Euro OTC	Calcium citrate tetrahydrate	1912013-01	1
Euro OTC	Calcium citrate tetrahydrate	1710007-01	1
Euro OTC	Calcium citrate tetrahydrate	1701001-01	2
Euro OTC	Calcium citrate tetrahydrate	1058904	1
Euro OTC	Calcium citrate tetrahydrate	1009030-01	1
Euro OTC	Calcium citrate tetrahydrate	3037086	1
Euro OTC	Calcium citrate tetrahydrate	1701001-02	1
Euro OTC	Calcium citrate tetrahydrate	1707025-01	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Calcium citrate tetrahydrate	1803031-02	2
Euro OTC	Calcium citrate tetrahydrate	1502021-02	1
Euro OTC	Calcium citrate tetrahydrate	1502012-01	1
Euro OTC	Calcium citrate tetrahydrate	1408017-01	4
Fagron	Calcium citrate tetrahydrate	13D16-N06	1
Fagron	Calcium citrate tetrahydrate	13d16-n06	1
Fagron	Calcium citrate tetrahydrate	150903901	1
Gatt-Koller	Calcium citrate tetrahydrate	1802139	3
Gehe Kassel	Calcium citrate tetrahydrate	14133307	1
Krieger	Calcium citrate tetrahydrate	17176808	1
L12	Calcium citrate tetrahydrate	1606001-03	1
lohmamm	Calcium citrate tetrahydrate	3045397	1
Noweda	Calcium citrate tetrahydrate	1509039-01	1
Noweda	Calcium citrate tetrahydrate	17176803	1
Euro OTC	Calcium citrate tetrahydrate	140801701	1
Caelo	Calcium citrate tetrahydrate	1716808	1
Phönix	Calcium citrate tetrahydrate	1305018-01	1
Caelo	Calcium citrate tetrahydrate	16056510	2
Sanacorp	Calcium citrate tetrahydrate	1211007-01	1
Sanacorp WE: 12.08.17 ...	Calcium citrate tetrahydrate	711105	1
Euro OTC	Calcium citrate tetrahydrate	1305018-02	1
Caelo	Calcium citrate tetrahydrate		2
Caelo	Calcium citrate tetrahydrate	13391203	4
Euro OTC	Calcium citrate tetrahydrate	1305018-01	3
Euro OTC	Calcium citrate tetrahydrate	1509039-01	2

- 111 047 spectra from 742 *Apo-Ident* customers from a total of 31 793 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium citrate tetrahydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium citrate tetrahydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	240	0	118 902
Type C	0	200	0	111 047

The substance/substance group *Calcium citrate tetrahydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 97.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium citrate tetrahydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	50.96	—
⋮	⋮	⋮
Cyanocobalamin	>50	98.04
Bacitracin	>50	105.18
Methylcobalamin	>50	159.84
Ethinylestradiol	>50	276.09

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium citrate tetrahydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21320	22995	4.32	46.33
22995	22995	0.00	46.75
21931	21931	0.00	43.88
22255	21931	1.40	43.44
21249	22995	3.17	44.21
23651	23651	0.00	51.58
21486	22995	3.46	46.04

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Calcium gluconate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20871-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Calcium gluconate; Calcii gluconas

Special notes

When selecting the *Calcium gluconate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium gluconate	6	5	52

Second-stage model

For differentiation of the substance/substance group *Calcium gluconate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium gluconate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium gluconate	12236502	20871	40	1401575
Caelo	Calcium gluconate	12335829	21312	40	20121121
Euro OTC	Calcium gluconate	1304012-01	21283	40	AR-15-FG-008127-01
Euro OTC	Calcium gluconate	1407041-01	21821	60	20140818
Euro OTC	Calcium gluconate	1911017	25086	40	20200123*
Euro OTC	Calcium gluconate	1712007	25106	40	20200203*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Calcium gluconate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Calcium gluconate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium gluconate	154356	23360	40
Caelo	Calcium gluconate	181010	24017	40
Caelo	Calcium gluconate	190240	24566	40
Euro OTC	Calcium gluconate	1606034	22699	40
Euro OTC	Calcium gluconate	1905015	24791	40
Euro OTC	Calcium gluconate	1712007	23873	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 135 spectra from 80 *Apo-Ident* customers from 54 batches from the substance/substance group *Calcium gluconate*.
- Among them are spectra of independent samples from 52 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Berkel AHK	Calcium gluconate	14085407	2
Caelo	Calcium gluconate	12335813	1
Caelo	Calcium gluconate	14085405	1
Caelo	Calcium gluconate	14230706	1
Caelo	Calcium gluconate	15324806	1
Caelo	Calcium gluconate	15435607	2
Caelo	Calcium gluconate	1606034	1
Caelo	Calcium gluconate	15435620	2
Caelo	Calcium gluconate	15435619	1
Caelo	Calcium gluconate	15435622	2
Caelo	Calcium gluconate	15435613	1
Caelo	Calcium gluconate	18101003	1
Caelo	Calcium gluconate	15324807	1
Caelo	Calcium gluconate	1407041-01	1
Caelo	Calcium gluconate	1712007-02	1
Caelo	Calcium gluconate	1543601	1
Caelo	Calcium gluconate	1712007_02	1
Caelo	Calcium gluconate	4(18101004)	1
Caelo	Calcium gluconate	12335810	1
Caelo	Calcium gluconate	15126301	1
Caelo	Calcium gluconate	16603401	1
Caelo	Calcium gluconate	18101004	3
Caelo	Calcium gluconate	18101010	1
Caelo	Calcium gluconate	1000041-01	1
Caelo	Calcium gluconate	140704102	1
Caelo	Calcium gluconate	15435601	2
Caelo	Calcium gluconate	15435611	1
EuRho	Calcium gluconate	1209006-01	2
EuRho	Calcium gluconate	1304012-01	1
EuRho	Calcium gluconate	12090006-01	1
Eurho/Sns	Calcium gluconate	1209006-01	1
Euro OTC	Calcium gluconate	115027-01	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Calcium gluconate	20270912-1	1
Euro OTC	Calcium gluconate	1209006-01	8
Euro OTC	Calcium gluconate	513-Q1211	1
Euro OTC	Calcium gluconate	1210001287	1
Euro OTC	Calcium gluconate	1304012-02	2
Euro OTC	Calcium gluconate	140704102	1
Euro OTC	Calcium gluconate	1606034-02	8
Euro OTC	Calcium gluconate	1602001644	2
Euro OTC	Calcium gluconate	1407041-02	9
Euro OTC	Calcium gluconate	140704101	1
Euro OTC	Calcium gluconate	1712007-02	2
Euro OTC	Calcium gluconate	130401202	1
Euro OTC	Calcium gluconate	1606034-01	13
Euro/Gehe	Calcium gluconate	1304012-01	1
Euro OTC	Calcium gluconate	1905015-01	4
Euro OTC	Calcium gluconate	1105027-01	1
Fagron	Calcium gluconate	12D17-N01	1
Fagron	Calcium gluconate	14D11-B04-294136	2
Fagron	Calcium gluconate	14D11-B04	1
Fagron	Calcium gluconate	10G22-N12	1
Fagron	Calcium gluconate	15D13-B98-307445	1
Finze	Calcium gluconate	917857359	1
Gatt-Koller / Phoenix	Calcium gluconate	550/03141214	1
GEHE	Calcium gluconate	15435619	1
Caelo	Calcium gluconate	1407041-02	1
Gehe/EuRo	Calcium gluconate	1712007-01	1
L12	Calcium gluconate	15435627	1
Euro OTC	Calcium gluconate	1105027-02	3
Pharmachem	Calcium gluconate	18101003	1
Phönix	Calcium gluconate	1606034-01	1
Caelo	Calcium gluconate	18106202	1
Phönix/Euro	Calcium gluconate	1606034-01	1
Euro OTC	Calcium gluconate	1712007-01	6
sanacorp	Calcium gluconate	1407041-01	1
Sidonia	Calcium gluconate	18101004	1
Euro OTC	Calcium gluconate	1407041-01	6
Euro OTC	Calcium gluconate	1304012-01	6

- 111 112 spectra from 742 *Apo-Ident* customers from a total of 31 837 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium gluconate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium gluconate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	240	0	118 902
Type C	0	127	8	111 112

The substance/substance group *Calcium gluconate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	94.0741 % (> 91.8519 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium gluconate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	22.40	—
Menthol	48.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium gluconate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21283	21283	0.00	24.72
21821	25106	4.04	24.22
25086	25086	0.00	23.53
25106	25106	0.00	26.08
20871	20871	0.00	25.77
21312	20871	5.38	25.93

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Calcium glycerophosphate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20352-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Calcium glycerophosphate; Calcii glycerophosphas

Special notes

When selecting the *Calcium glycerophosphate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium glycerophosphate	5	4	44

Second-stage model

For differentiation of the substance/substance group *Calcium glycerophosphate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium glycerophosphate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium glycerop...	13007912	21311	40	20130124
Caelo	Calcium glycerop...	14341007	21969	60	AR-16-FG-005932-01
Caelo	Calcium glycerop...	191007	24538	40	20190502*
Fagron	Calcium glycerop...	13I17-N04	21234	40	20131016
Fagron	Calcium glycerop...	15B03-B03-305050	21978	60	1706313

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Calcium glycerophosphate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Calcium glycerophosphate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium glycerophosphate	12012411	20679	40
Caelo	Calcium glycerophosphate	12012417	20762	40
Caelo	Calcium glycerophosphate	12012413	20763	40
Caelo	Calcium glycerophosphate	162310	23361	40
Caelo	Calcium glycerophosphate	12012417	20771	40

- 118 942 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 101 spectra from 68 *Apo-Ident* customers from 47 batches from the substance/substance group *Calcium glycerophosphate*.
- Among them are spectra of independent samples from 44 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Calcium glycerophosphate	12012406	1
Caelo	Calcium glycerophosphate	12012413	2
Caelo	Calcium glycerophosphate	13A18-No2	1
Caelo	Calcium glycerophosphate	13007908	1
Caelo	Calcium glycerophosphate	14347101	2
Caelo	Calcium glycerophosphate	16231001	3
Caelo	Calcium glycerophosphate	16231006	3
Caelo	Calcium glycerophosphate	162310	1
Caelo	Calcium glycerophosphate	16231007	2
Caelo	Calcium glycerophosphate	16231010	4
Caelo	Calcium glycerophosphate	17359101	8
Caelo	Calcium glycerophosphate	180918A	1
Caelo	Calcium glycerophosphate	17359107	5
Caelo	Calcium glycerophosphate	19100701	1
Caelo	Calcium glycerophosphate	19100703	5
Caelo	Calcium glycerophosphate	17250703	3
Caelo	Calcium glycerophosphate	14341010	1
Caelo	Calcium glycerophosphate	16231005	1
Caelo	Calcium glycerophosphate	14341013	1
Caelo	Calcium glycerophosphate	13007914	1
Caelo	Calcium glycerophosphate	15B03B03305050	1
Caelo	Calcium glycerophosphate	14B10-B02-296841	1
Caelo	Calcium glycerophosphate	14341009	1
Caelo	Calcium glycerophosphate	16231008	1
Caelo	Calcium glycerophosphate	15B03-B03-305050	1
Caelo	Calcium glycerophosphate	16231004	2
Caelo	Calcium glycerophosphate	14341015	1
Caelo/Sanacorp	Calcium glycerophosphate	17359101	1
Fagron	Calcium glycerophosphate	11G19-N05	1
Fagron	Calcium glycerophosphate	12I18-N06	3
Fagron	Calcium glycerophosphate	1216000005	1
Fagron	Calcium glycerophosphate	13A18N02	2
Fagron	Calcium glycerophosphate	13A18-N02	5

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Supplier	Substance	Batch	Spectra
Fagron	Calcium glycerophosphate	1317-N04	2
Fagron	Calcium glycerophosphate	1314000019	1
Fagron	Calcium glycerophosphate	14B10B02	1
Fagron	Calcium glycerophosphate	15B03B03	1
Fagron	Calcium glycerophosphate	14B10-B02	1
Fagron	Calcium glycerophosphate	15B03-B03	1
Fagron	Calcium glycerophosphate	17J17-B07-3583	1
Fagron	Calcium glycerophosphate	14B10-B02-291642	1
Fagron	Calcium glycerophosphate	14B10-B02-296841	4
Fagron	Calcium glycerophosphate	5212M-01212	1
Fagron	Calcium glycerophosphate	3115A-01212	1
Gatt-Koller/Kwizda	Calcium glycerophosphate	4007/09123812	1
Gehe	Calcium glycerophosphate	19100703	1
Caelo	Calcium glycerophosphate	13007902	1
Caelo	Calcium glycerophosphate	17359106	4
Sidonia	Calcium glycerophosphate	17250703	1
Caelo	Calcium glycerophosphate	13007912	2
Caelo	Calcium glycerophosphate	14341007	5
Fagron	Calcium glycerophosphate	15B03-B03-305050	3

- 111 146 spectra from 742 *Apo-Ident* customers from a total of 31 845 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium glycerophosphate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium glycerophosphate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	200	0	118 942
Type C	0	95	6	111 146

The substance/substance group *Calcium glycerophosphate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	94.0594 % (> 91.0891 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium glycerophosphate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Polymyxin B sulfate	28.74	—
Magnesium citrate	44.66	—
Carmellose sodium (400 / 450 / 500 / 6...	45.46	—
Levothyroxin sodium	46.83	—
Calcium citrate tetrahydrate	47.80	—
Aciclovir	47.97	—
Menthol	49.39	—
Arginine hydrochloride	51.74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium glycerophosphate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24538	24538	0.00	33.42
21978	21978	0.00	29.09
21234	21969	8.84	37.62
21311	21969	5.47	38.75
21969	21969	0.00	34.38

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Calcium lactate pentahydrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20745-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Calcium lactate pentahydrate; Calcii lactas pentahydricus

Special notes

When selecting the *Calcium lactate pentahydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium lactate pentahydrate	5	3	31

Second-stage model

For differentiation of the substance/substance group *Calcium lactate pentahydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium lactate pentahydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium lactate ...	15101401	21909	60	20150407
Caelo	Calcium lactate ...	15101405	22263	60	20150407
Caelo	Calcium lactate ...	161313	22445	60	20160513*
Fagron	Calcium lactate ...	12E10-N03	20745	40	20120704
Fagron	Calcium lactate ...	12I12-N06	21232	40	AR-15-FG-007939-01

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *Calcium lactate pentahydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Calcium lactate pentahydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium lactate pentahydrate	171377	23642	40
Caelo	Calcium lactate pentahydrate	180734	24035	40
Fagron	Calcium lactate pentahydrate	14H01-B05-323830	23566	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 56 spectra from 21 *Apo-Ident* customers from 33 batches from the substance/substance group *Calcium lactate pentahydrate*.
- Among them are spectra of independent samples from 31 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Calcium lactate pentahydrate	12E10-N03	1
Caelo	Calcium lactate pentahydrate	12C15-N02	1
Caelo	Calcium lactate pentahydrate	11369610	1
Caelo	Calcium lactate pentahydrate	11369614	2
Caelo	Calcium lactate pentahydrate	13080802	2
Caelo	Calcium lactate pentahydrate	13080804	2
Caelo	Calcium lactate pentahydrate	13080805	2
Caelo	Calcium lactate pentahydrate	17355503	1
Caelo	Calcium lactate pentahydrate	11369618	1
Caelo	Calcium lactate pentahydrate	16131312	1
Caelo	Calcium lactate pentahydrate	16131302	1
Caelo	Calcium lactate pentahydrate	14H01B05300502	1
Caelo	Calcium lactate pentahydrate	18073413	2
Caelo	Calcium lactate pentahydrate	16131307	1
Caelo	Calcium lactate pentahydrate	11369606	1
Caelo	Calcium lactate pentahydrate	15227804	2
Caelo	Calcium lactate pentahydrate	15101409	1
Caelo	Calcium lactate pentahydrate	15101411	2
Caelo	Calcium lactate pentahydrate	15101412	3
Caelo	Calcium lactate pentahydrate	16333106	4
Caelo	Calcium lactate pentahydrate	16333111	4
Caelo	Calcium lactate pentahydrate	17137707	2
Fagron	Calcium lactate pentahydrate	12C15-N02	1
Fagron	Calcium lactate pentahydrate	12I12-N01	1
Fagron	Calcium lactate pentahydrate	13L18B04	1
Fagron	Calcium lactate pentahydrate	14H01-B05-334588	1
Fagron	Calcium lactate pentahydrate	13L18-B04-295541	3
Fagron	Calcium lactate pentahydrate	1806000537	1
Fagron	Calcium lactate pentahydrate	12/12-N06	1
Fagron	Calcium lactate pentahydrate	17J18-B01-347174	1
Fagron	Calcium lactate pentahydrate	14H01-B05	1
Caelo	Calcium lactate pentahydrate	18073406	2
phönix	Calcium lactate pentahydrate	15101411	1
Phönix	Calcium lactate pentahydrate	14H01-B05	1
Shop	Calcium lactate pentahydrate	1111001829	1
Fagron	Calcium lactate pentahydrate	12I12-N06	2

- 111 191 spectra from 742 *Apo-Ident* customers from a total of 31 858 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium lactate pentahydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium lactate pentahydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	56	0	111 191

The substance/substance group *Calcium lactate pentahydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 89.2857 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium lactate pentahydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium citrate	36.74	—
Menthol	37.71	—
Tartaric acid	44.55	—
Levothyroxin sodium	44.83	—
Riboflavin phosphate sodium	45.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium lactate pentahydrate* is separated from critical neighbours in a

second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22445	22445	0.00	23.28
20745	22445	4.05	24.47
21232	21232	0.00	22.45
21909	22445	4.82	26.02
22263	22445	3.78	20.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Calcium orotate dihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20418-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Calcium orotate dihydrate; Calcii orotas dihydricus

Special notes

When selecting the *Calcium orotate dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium orotate dihydrate	4	3	1

Second-stage model

For differentiation of the substance/substance group *Calcium orotate dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium orotate dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Calcium orotate ...	1401006-01	21245	40	1412540
Euro OTC	Calcium orotate ...	1603003	22520	40	20160329*
Euro OTC	Calcium orotate ...	1603003	24164	40	20180615*
Fagron	Calcium orotate ...	12L04-N07	20824	40	20121207
Fagron	Calcium orotate ...	13J23-N05	21227	40	20131111

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Calcium orotate dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110489 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Calcium orotate dihydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Calcium orotate dihydrate	1009035-01	20814	40
Euro OTC	Calcium orotate dihydrate	1411003	22519	40
Fagron	Calcium orotate dihydrate	16F13-B04-324144	23574	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Calcium orotate dihydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Calcium orotate dihydrate	1203037-01	2
Euro OTC	Calcium orotate dihydrate	1401006-01	1

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium orotate dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium orotate dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	80	40	119 022
Type C	0	3	0	111 244

The substance/substance group *Calcium orotate dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	66.6667 % (> 64.1667 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium orotate dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	42.54	—
Levothyroxin sodium	74.10	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium orotate dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20824	21245	1.49	65.62
21227	21245	2.87	65.75
21245	21245	0.00	66.68
22520	22520	0.00	95.35
24164	24164	0.00	95.67

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Calcium pantothenate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20395-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Calcium pantothenate; Calcii panthothenicum

Special notes

When selecting the *Calcium pantothenate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Calcium pantothenate	9	5	42

Second-stage model

For differentiation of the substance/substance group *Calcium pantothenate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Calcium pantothenate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Calcium pantothe...	14208012	21765	60	20140722
Caelo	Calcium pantothe...	173352	24045	40	20180202*
Euro OTC	Calcium pantothe...	1305034-01	21243	40	20130617
Euro OTC	Calcium pantothe...	1509024	21901	60	20151005*
Euro OTC	Calcium pantothe...	1603042	22551	40	20160429*
Euro OTC	Calcium pantothe...	1607023	22691	40	20160809*
Euro OTC	Calcium pantothe...	1702018	23153	40	20170330*
Euro OTC	Calcium pantothe...	1711003	23890	40	20171123*
Fagron	Calcium pantothe...	13H28-N11	21233	40	20130916

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 9 reference samples from the substance/substance group *Calcium pantothenate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 289 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Calcium pantothenate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Calcium pantothenate	162516	23363	40
Caelo	Calcium pantothenate	15344217	23717	40
Euro OTC	Calcium pantothenate	1803014	24081	40
Euro OTC	Calcium pantothenate	1809014	24312	40
Euro OTC	Calcium pantothenate	1902032	24479	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 85 spectra from 47 *Apo-Ident* customers from 45 batches from the substance/substance group *Calcium pantothenate*.
- Among them are spectra of independent samples from 42 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Calcium pantothenate	15344221	1
Anzag/Anzag 26.07.18	Calcium pantothenate	1803017-01	1
Fagron	Calcium pantothenate	1111025-01	1
Caelo	Calcium pantothenate	1013Q-03022	1
Caelo	Calcium pantothenate	27111303	1
Caelo	Calcium pantothenate	12340819	2
Caelo	Calcium pantothenate	8041407	1
Caelo	Calcium pantothenate	15344207	1
Caelo	Calcium pantothenate	1509024-01	1
Caelo	Calcium pantothenate	16251608	2
Caelo	Calcium pantothenate	19067405	2
Caelo	Calcium pantothenate	1711003-01	1
Caelo	Calcium pantothenate	14208004	1
Caelo	Calcium pantothenate	12340859	1
Caelo	Calcium pantothenate	11105731	1
Caelo	Calcium pantothenate	15344214	1
Caelo	Calcium pantothenate	12340808	3
Caelo	Calcium pantothenate	1410011-01	1
Caelo	Calcium pantothenate	1410011-02	1
Caelo	Calcium pantothenate	12236622	1
Caelo	Calcium pantothenate	12340809	1
Caelo	Calcium pantothenate	12340846	1
Caelo	Calcium pantothenate	17335208	4
Caelo	Calcium pantothenate	12340832	1
Euro OTC	Calcium pantothenate	190203202	1
Euro OTC	Calcium pantothenate	130503401	2
Euro OTC	Calcium pantothenate	17021401	1
Euro OTC	Calcium pantothenate	10021505	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Calcium pantothenate	1410011-02	3
Euro OTC	Calcium pantothenate	18111707	1
Euro OTC	Calcium pantothenate	1711003-01	6
Euro OTC	Calcium pantothenate	1803014-01	3
Euro OTC	Calcium pantothenate	1312027-01	3
Euro OTC	Calcium pantothenate	1209022-01	1
Euro OTC	Calcium pantothenate	1702018-01	2
Euro OTC	Calcium pantothenate	1410011-01	1
Euro OTC	Calcium pantothenate	1607023-01	5
Euroo/Anzag	Calcium pantothenate	1509024-01	2
Euro OTC	Calcium pantothenate	1111025-01	1
Euro OTC	Calcium pantothenate	1603042-01	4
Euro OTC	Calcium pantothenate	1209022-02pzn	1
Fagron	Calcium pantothenate	1111110405	1
Fagron	Calcium pantothenate	14G02-B10-297373	1
Fagron	Calcium pantothenate	12F19-N07	1
Gehe	Calcium pantothenate	1004024-01	1
Noweda	Calcium pantothenate	14208012	1
Euro OTC	Calcium pantothenate	1209022-02	1
Euro OTC	Calcium pantothenate	5121405	1
Euro OTC	Calcium pantothenate	1509024-01	3
Euro OTC	Calcium pantothenate	1305034-01	4
Fagron	Calcium pantothenate	13H28-N11	1

- 111 162 spectra from 742 *Apo-Ident* customers from a total of 31 847 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Calcium pantothenate* can be clearly distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Calcium pantothenate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	200	0	118 942
Type C	0	84	1	111 162

The substance/substance group *Calcium pantothenate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	98.8235 % (> 95.2941 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Calcium pantothenate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Polymyxin B sulfate	17.70	—
Citrulline	18.02	—
Colistin sulfate	21.23	—
Bacitracin	26.35	—
Magnesium citrate	26.46	—
Amphotericin B	38.08	—
Riboflavin	41.94	—
Clindamycin hydrochloride	43.05	—
Levothyroxin sodium	44.20	—
Minoxidil	45.43	—
Calcium citrate tetrahydrate	45.77	—
Cyanocobalamin	48.91	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Calcium pantothenate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21233	23153	7.04	20.86
21243	24045	5.31	21.85
22691	22691	0.00	15.31
21765	24045	6.85	22.60
23153	23153	0.00	20.75
23890	23890	0.00	19.97
24045	24045	0.00	21.30
22551	22551	0.00	15.00
21901	21901	0.00	18.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Camphor, racemic**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 25048-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Camphor, racemic

Special notes

When selecting the *Camphor, racemic* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Camphor, racemic	5	5	5

Second-stage model

For differentiation of the substance/substance group *Camphor, racemic* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Camphor, racemic*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Camphor, racemic	15316801	25049	60	20151029
Caelo	Camphor, racemic	170043	25051	40	20170220*
Euro OTC	Camphor, racemic	1406029-01	25048	60	20140708
Fagron	Camphor, racemic	14E19-B07-300365	25050	60	20140527
Fagron	Camphor, racemic	16E23-B08-336937	25053	40	20160627

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *Camphor, racemic*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Camphor, racemic*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Camphor, racemic	183279	24728	40
Caelo	Camphor, racemic	192454	24876	40
Caelo	Camphor, racemic	16209309	25052	40
Caelo	Camphor, racemic	172883	25054	40
Caelo	Camphor, racemic	180198	25055	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 8 *Apo-Ident* customers from 5 batches from the substance/substance group *Camphor, racemic*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Camphor, racemic	17288306	1
Caelo	Camphor, racemic	18327905	3
Caelo	Camphor, racemic	18327909	3
Caelo	Camphor, racemic	17050605	1
Klenk	Camphor, racemic	444A180815	5

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Camphor, racemic* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Camphor, racemic* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	200	0	118 862
Type C	0	13	0	110 683

The substance/substance group *Camphor, racemic* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8898 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Camphor*, *racemic* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol valerate	34.31	—
Finasteride (form III)	47.33	—
Budesonide, micronized	48.87	—
Dexamethasone	57.20	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Camphor*, *racemic* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
25048	25051	23.48	49.17
25049	25051	10.20	48.87
25050	25051	19.48	49.95
25051	25051	0.00	49.12
25053	25051	13.80	49.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Cannabidiol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22416-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cannabidiol

Special notes

When selecting the *Cannabidiol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cannabidiol	4	1	47

Second-stage model

For differentiation of the substance/substance group *Cannabidiol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cannabidiol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22412	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22412SI	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22413	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22414	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22415	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22416	60	1316Q-07806
THC-Pharma GmbH	Cannabidiol	CBD-API17-003	23398	40	20170609
THC-Pharma GmbH	Cannabidiol	CBD-API17-003	23399	40	20170609
THC-Pharma GmbH	Cannabidiol	CBD-API16-003	23464	40	2017B-03911
THC-Pharma GmbH	Cannabidiol	CBD-API16-004	23465	40	2017A-03911

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 520 spectra of 10 reference samples from the substance/substance group *Cannabidiol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 169 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 471 spectra of 10 reference samples from the substance/substance group *Cannabidiol*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
THC-Pharma GmbH	Cannabidiol	CBD-API1801	23929	40
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22413SI [†]	60
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22414SI [†]	60
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22415SI [†]	60
THC-Pharma GmbH	Cannabidiol	15-7221-80338	22416SI [†]	60
THC-Pharma GmbH	Cannabidiol	CBD-API17-003	23398SI [†]	40
THC-Pharma GmbH	Cannabidiol	CBD-API17-003	23399SI [†]	31
THC-Pharma GmbH	Cannabidiol	CBD-API16-003	23464SI [†]	40
THC-Pharma GmbH	Cannabidiol	CBD-API16-004	23465SI [†]	40
THC-Pharma GmbH	Cannabidiol	CBD-API1801	23929SI	40

- 118671 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 298 spectra from 37 *Apo-Ident* customers from 52 batches from the substance/substance group *Cannabidiol*.
- Among them are spectra of independent samples from 25 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
alpha-Cannabis Pharma ...	Cannabidiol	ACPL418001	1
alpha-cannabis Pharma G...	Cannabidiol	ACPK911004	3
alpha-cannabis Pharma G...	Cannabidiol	ACPK012405	1
Apocare	Cannabidiol	ACPK911004	9
Apocare	Cannabidiol	ACPK312001	1
APOCARE Pharma GmbH	Cannabidiol	ACPL418001	1
APOCARE Pharma GmbH	Cannabidiol	ACPL416001	3
Caelo	Cannabidiol	110216-02	3
Caelo	Cannabidiol	CBD-API1803	1
Caelo	Cannabidiol	CBD-API17-006	2
Caelo	Cannabidiol	CBD-API1801	2
Laborchemie APOLDA GmbH	Cannabidiol	APCK312001	1
Pharmachem GmbH & Co. KG	Cannabidiol	CBD-API1801	2
Sanacorp	Cannabidiol	CBD-API1804	3
THC	Cannabidiol	CBD-API17-002	2
THC	Cannabidiol	CBD-API17-003	1
THC	Cannabidiol	CBD-API17-004	4
THC	Cannabidiol	CBD-API17-006	2
THC Pharm	Cannabidiol	CBD-API16-004	1
THC Pharm	Cannabidiol	CBD-API17-004	1
THC Pharm	Cannabidiol	CBD-API1708	1
THC Pharm	Cannabidiol	H150218-1	1
THC Pharm	Cannabidiol	CBD-API1802	1
THC Pharm	Cannabidiol	CBD-API1804	4

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
THC Pharm	Cannabidiol	10C170619-1	1
THC Pharm	Cannabidiol	CBD-API1901	1
THC Pharm GmbH	Cannabidiol	CBD-API17-005	3
THC Pharm GmbH	Cannabidiol	CBD-API17-006	2
THC Pharm GmbH	Cannabidiol	CBD-API1707	2
THC Pharm GmbH	Cannabidiol	CBD-API1801	3
THC Pharm GmbH	Cannabidiol	CBD-API1802	1
THC Pharm GmbH	Cannabidiol	CBD-API1804	2
THC Pharm GmbH / THC Ph...	Cannabidiol	CBD-API17-005	1
THC Pharma	Cannabidiol	CBD-API16-004	3
THC Pharma	Cannabidiol	CBD-API17-002	5
THC Pharma	Cannabidiol	CBD-API17-005	6
THC Pharma	Cannabidiol	CBD-API17-004	9
THC Pharma	Cannabidiol	CBD-API1707	2
THC Pharma	Cannabidiol	CBD-API1706	4
THC Pharma	Cannabidiol	CBD-API1801	1
THC Pharma	Cannabidiol	CBD-API1804	5
THC Pharma	Cannabidiol	CBD-API1802	2
THC Pharma (direkt)	Cannabidiol	CBD-API17-006	1
THC Pharma (direkt)	Cannabidiol	CBD-API1707	1
THC Pharma (direkt)	Cannabidiol	CBD-API1708	1
THC Pharma (direkt)	Cannabidiol	CBD-API1801	1
THC/ Direkt	Cannabidiol	CBD-API1706	1
THC/Gehe	Cannabidiol	CBD-API17-005	1
THC-Pharm	Cannabidiol	cbd-adi17-002	1
THC-Pharm	Cannabidiol	CBD-API17-003	3
THC-Pharm	Cannabidiol	CBD-API17-005	1
THC-Pharm	Cannabidiol	CBD-API17-004	1
THC-Pharma	Cannabidiol	CBD-API17-003	1
THC-Pharma	Cannabidiol	CBD-API1708	1
THC-Pharma	Cannabidiol	CBD-API1708	1
THC-Pharma	Cannabidiol	CBD-API1804	1
THC-Pharma	Cannabidiol	CBD-API1802	1
Bombastus	Cannabidiol		1
Euro OTC	Cannabidiol		3
Pharmachem GmbH & Co. KG	Cannabidiol		4
Sanacorp	Cannabidiol		6
THC	Cannabidiol		2
Thc Pharm	Cannabidiol		1
THC Pharm	Cannabidiol		22
thc pharm gmbh	Cannabidiol		3
THC Pharm GmbH	Cannabidiol		23
THC Pharm/ Sanacorp	Cannabidiol		16
THC Pharm/ THC Pharm	Cannabidiol		2
THC Pharm/ THC Pharm GmbH	Cannabidiol		1
THC pharma	Cannabidiol		2
THC Pharma	Cannabidiol		64
THC Pharma (direkt)	Cannabidiol		2
THC-Pharm	Cannabidiol		12
THC-Pharma	Cannabidiol		13

- 110 949 spectra from 742 *Apo-Ident* customers from a total of 31 839 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cannabidiol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cannabidiol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	520	0	110 169
Type B	0	471	0	118 671
Type C	0	297	1	110 949

The substance/substance group *Cannabidiol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8462 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.7261 %)
Type C	100.0000 % (> 99.8899 %)	99.6644 % (> 98.6577 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cannabidiol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estriol	43.32	–
Prednisolon dihydrogen phosphate dinat. . .	56.16	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cannabidiol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22412	22412	0.00	43.32
22413	22413	0.00	44.30
22414	22414	0.00	44.38
22415	22415	0.00	44.44
22416	22416	0.00	43.62
23398	22413	2.77	45.56
23399	22413	2.63	46.16
23464	23464	0.00	47.17
23465	23465	0.00	44.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Capsaicin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20854-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Capsaicin; Capsaicinoida

Special notes

When selecting the *Capsaicin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Capsaicin	3	6	7

Second-stage model

For differentiation of the substance/substance group *Capsaicin* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Capsaicin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Capsaicin	1703023	23145	40	20170407*
Euro OTC	Capsaicin	1811009	24331	40	20181207*
Fagron	Capsaicin	13J07-N07	21340	40	AR-15-FG-007151-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Capsaicin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 300 spectra of 7 reference samples from the substance/substance group *Capsaicin*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Capsaicin	118066-04	21638	60
Euro OTC	Capsaicin	1603005-01	22930	40
Euro OTC	Capsaicin	1806013-01	24186	40
Euro OTC	Capsaicin	1812015	24457	40
Euro OTC	Capsaicin	1903032	24638	40
Fagron	Capsaicin	13D12-N01	20854	40
Euro OTC	Capsaicin	1603005-01	22931	40

- 118 842 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 22 spectra from 13 *Apo-Ident* customers from 7 batches from the substance/substance group *Capsaicin*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
EuRho	Capsaicin	1703023-02	1
Euro OTC	Capsaicin	1401043-02	2
Euro OTC	Capsaicin	1703023-025346	1
Euro OTC	Capsaicin	1812015-01	1
Euro OTC	Capsaicin	1806013-01	2
Euro OTC	Capsaicin	1603005-01	13
Euro OTC	Capsaicin	1703023-02	1
Fagron	Capsaicin	CP-12003	1

- 111 225 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Capsaicin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Capsaicin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	300	0	118 842
Type C	0	20	2	111 225

The substance/substance group *Capsaicin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.0000 %)
Type C	100.0000 % (> 99.8899 %)	90.9091 % (> 77.2727 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Capsaicin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	15.33	—
Cyanocobalamin	27.72	—
Prednisolon dihydrogen phosphate dinat...	29.62	—
Estradiol hemihydrate	33.25	—
Prednisone	34.23	64.16
Methylcobalamin	34.42	—
Minoxidil	36.41	—
Polymyxin B sulfate	39.35	—
Nystatin	40.41	—
Magnesium citrate	41.55	—
L-glutathione	42.85	—
Calcium citrate tetrahydrate	48.17	—
Colistin sulfate	49.79	—
Glycyrrhizic acid	50.26	—
:	:	:
Triamcinolone acetonide	>50	105.18
Dexamethasone	>50	113.00
Betamethasone valerate	>50	131.57
Prednisolone, micronized	>50	155.31
Betamethasone, micronized	>50	163.04
Budesonide, micronized	>50	178.27
Erythromycin	>50	178.90
Prednicarbate, micronized	>50	199.93
Triamcinolone, micronized	>50	201.64
Norethisterone acetate	>50	231.30
Heparin sodium	>50	351.15

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Capsaicin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21340	21340	0.00	16.47
24331	24331	0.00	20.73
23145	23145	0.00	15.33

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Captopril**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20890-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Captopril; Captoprilum

Special notes

When selecting the *Captopril* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Captopril	5	3	91

Second-stage model

For differentiation of the substance/substance group *Captopril* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Captopril*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Captopril	12339610	21064	40	1403227
Caelo	Captopril	15189502	21874	60	AR-15-FG-014855-01
Caelo	Captopril	190118	24546	40	20190312*
Fagron	Captopril	12G25-N08	20890	40	20120814
Fagron	Captopril	14B26-B01-312221	21921	60	20140317

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Captopril*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 310 spectra of 7 reference samples from the substance/substance group *Captopril*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Captopril	170772	23366	40
Caelo	Captopril	172102	23676	40
Fagron	Captopril	17G21-B02-337989	23588	30
Caelo	Captopril	15189502	21874SI [†]	60
Caelo	Captopril	170772	23366SI	40
Caelo	Captopril	190118	24546SI [†]	40
Fagron	Captopril	14B26-B01-312221	21921SI [†]	60

- 118 832 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 283 spectra from 118 *Apo-Ident* customers from 97 batches from the substance/substance group *Captopril*.
- Among them are spectra of independent samples from 91 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Captopril	17210202	1
Caelo	Captopril	12339602	1
Caelo	Captopril	15189503	1
Caelo	Captopril	14B26-B40-318894	1
Caelo	Captopril	12339605	4
Caelo	Captopril	12339619	1
Caelo	Captopril	14196904	8
Caelo	Captopril	15189501	6
Caelo	Captopril	14B26-B01-310127	2
Caelo	Captopril	15189511	5
Caelo	Captopril	15189514	6
Caelo	Captopril	15189510	2
Caelo	Captopril	15189515	1
Caelo	Captopril	15189517	5
Caelo	Captopril	15189519	2
Caelo	Captopril	16B26-B01310127	1
Caelo	Captopril	15189524	2
Caelo	Captopril	1519521	1
Caelo	Captopril	17077201	3
Caelo	Captopril	17077202	4
Caelo	Captopril	17077205	1
Caelo	Captopril	17077206	1
Caelo	Captopril	17210202	10
Caelo	Captopril	18058003	1
Caelo	Captopril	18058006	2
Caelo	Captopril	18058007	1
Caelo	Captopril	18058005	4

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Captopril	18058009	1
Caelo	Captopril	19011802	2
Caelo	Captopril	19011807	1
Caelo	Captopril	190118001	1
Caelo	Captopril	15189509	2
Caelo	Captopril	14B26-B40-320183	1
Caelo	Captopril	12339604	2
Caelo	Captopril	15189512	7
Caelo	Captopril	5102-14-042	1
Caelo	Captopril	18058002	3
Caelo	Captopril	14B26-B01-310127	1
Caelo	Captopril	14B26-B40	1
Caelo	Captopril	18058004	5
Caelo	Captopril	14B26-B40-325275	2
Caelo	Captopril	17210205	9
Caelo	Captopril	14196903	2
Caelo	Captopril	14B26-B01-291555	1
Caelo	Captopril	14B26-B40-323267	1
Caelo	Captopril	15189526	2
Caelo	Captopril	17210201	2
Caelo	Captopril	12339616	2
Caelo	Captopril	14196905	3
Caelo	Captopril	14196901	1
Caelo	Captopril	17077209	12
Caelo	Captopril	12339617	1
Caelo	Captopril	15189521	5
Caelo	Captopril	15189525	2
Caelo	Captopril	17077208	8
Caelo	Captopril	17G27-B02	2
Caelo	Captopril	17210204	2
Caesar & Loretz GmbH	Captopril	19011802	1
Caesar&Loretz	Captopril	17210201	1
Cealo/Sanacorp	Captopril	12339617	1
Changzhou Pharmaceutical	Captopril	14B26-B40-321319	1
Euro OTC	Captopril	15189507	3
Euro OTC	Captopril	14B26-B40-320183	1
Euroct/Gehe	Captopril	14B26-B40-320183	1
Euro OTC	Captopril	17210204	1
Fagron	Captopril	12K16-N04	1
Fagron	Captopril	14B26-B01-291555	3
Fagron	Captopril	14B26-B01	6
Fagron	Captopril	14B26-B01-291557	5
Fagron	Captopril	14B26-B01_2911557	1
Fagron	Captopril	80616-6	1
Fagron	Captopril	14B26-W0129-1557	1
Fagron	Captopril	14B26B01	1
Fagron	Captopril	EC140101	1
Fagron	Captopril	14B26-B01-314460	1
Fagron	Captopril	14B26-B01-316257	2
Fagron	Captopril	14B26-B40-320183	6
Fagron	Captopril	700766	1
Fagron	Captopril	14B26-B01-302337	1
Fagron	Captopril	14B26-B40-325275	3
Fagron	Captopril	17g27-b02-337989	1
Fagron	Captopril	14B26-B40-323267	3
Fagron	Captopril	17G27-B02-340798	2
Fagron	Captopril	17G27-B02-346203	2
Fagron	Captopril	17G27-B02-356147	3
Fagron	Captopril	17G27-B02-350997	1
Fagron	Captopril	14B26-B01-291556	3

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Supplier	Substance	Batch	Spectra
Fagron	Captopril	14B26-B40-321319	4
Fagron	Captopril	17G27-B02-337989	3
Fagron	Captopril	12K-16N04	1
Fagron	Captopril	14196902	1
Fagron	Captopril	19I24-F01-365391	1
Fagron	Captopril	14B26-B01_302338	1
Fagron	Captopril	14B26-B01-302338	2
Fagron	Captopril	14B26-B01-310127	2
Fagron	Captopril	14B26-B40-318894	5
Fagron	Captopril	17G27-B02-352730	2
Fagron	Captopril	17G-B02-352730	1
Fagron	Captopril	14B26-B01-310127	2
Gehe	Captopril	18058002	1
Gehe	Captopril	18058004	2
Gehe	Captopril	18058010	1
Gehe	Captopril	19011805	2
GEHE	Captopril	17210203	1
GEHE	Captopril	17077209	1
GEHE	Captopril	18058003	1
Caelo	Captopril	14B26-B01-291557	1
Hedinger	Captopril	14B26-B40	2
Herstellung	Captopril	12339607	1
Klosterring	Captopril	17G27-B02-340471	1
Caelo	Captopril	1805005	1
L12	Captopril	17077202	2
Noweda	Captopril	17210202	1
Phonix	Captopril	14B26-B01	1
Phönix	Captopril	18058002	1
Caelo	Captopril	19011801	4
Sonnenberg-Apotheke	Captopril	14B26-B01-291557	2
THC Pharma	Captopril	18058002	1
Caelo	Captopril	12F29-N04	1
Caelo	Captopril	12339610	2
Caelo	Captopril	15189502	1
Fagron	Captopril	12G25-N08	4
Fagron	Captopril	14B26-B01-312221	1
	Captopril		1

- 110 964 spectra from 742 *Apo-Ident* customers from a total of 31 797 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Captopril* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Captopril* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	310	0	118 832
Type C	0	278	5	110 964

The substance/substance group *Captopril* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.0645 %)
Type C	100.0000 % (> 99.8899 %)	98.2332 % (> 97.1731 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Captopril* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ofloxacin	22.94	–
Estriol	48.86	–
Pilocarpine hydrochloride	62.98	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Captopril* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21874	21874	0.00	34.45
21921	21874	6.13	36.64
20890	21064	2.04	38.43
21064	21064	0.00	37.53
24546	24546	0.00	38.42

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Carbomers 35000 / 50000**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20548-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Carbomers 35000 / 50000

Special notes

When selecting the *Carbomers 35000 / 50000* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Carbomers 35000 / 50000	10	12	126

Second-stage model

For differentiation of the substance/substance group *Carbomers 35000 / 50000* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Carbomers 35000 / 50000*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Carbomers 35000 ...	13135601	20978	40	1403767
Caelo	Carbomers 35000 ...	13186207	20979	40	1403768
Caelo	Carbomers 35000 ...	14057902	21354	40	20140228
Caelo	Carbomers 35000 ...	14057903	21557	60	20140228
Caelo	Carbomers 35000 ...	162530	22759	40	20161011*
Euro OTC	Carbomers 35000 ...	1311027-02	21561	60	20131205
Euro OTC	Carbomers 35000 ...	1512010	22250	60	20151216*
Euro OTC	Carbomers 35000 ...	1604032	22548	40	20160428*
Euro OTC	Carbomers 35000 ...	1607028	22686	40	20160804*
Euro OTC	Carbomers 35000 ...	1610024	22852	40	20161102*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 10 reference samples from the substance/substance group *Carbomers 35000 / 50000*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 229 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 480 spectra of 12 reference samples from the substance/substance group *Carbomers 35000 / 50000*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Carbomers 35000 / 50000	172520	23621	40
Caelo	Carbomers 35000 / 50000	173614	23783	40
Caelo	Carbomers 35000 / 50000	180924	24250	40
Caelo	Carbomers 35000 / 50000	183074	24543	40
Caelo	Carbomers 35000 / 50000	190245	24565	40
Euro OTC	Carbomers 35000 / 50000	1702012	23139	40
Euro OTC	Carbomers 35000 / 50000	1706015	23534	40
Euro OTC	Carbomers 35000 / 50000	1801044	23959	40
Euro OTC	Carbomers 35000 / 50000	1810019	24315	40
Euro OTC	Carbomers 35000 / 50000	1903007	24468	40
Euro OTC	Carbomers 35000 / 50000	1908029	24858	40
Euro OTC	Carbomers 35000 / 50000	2003049	25124	40

- 118 662 spectra from a total of 2408 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 427 spectra from 256 *Apo-Ident* customers from 132 batches from the substance/substance group *Carbomers 35000 / 50000*.
- Among them are spectra of independent samples from 125 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance H.	Carbomers 35000 / 50000	1512010-01	1
Caelo	Carbomers 35000 / 50000	15015709	2
Caelo	Carbomers 35000 / 50000	18307406	2
Caelo	Carbomers 35000 / 50000	11351623	1
Caelo	Carbomers 35000 / 50000	11351605	3
Caelo	Carbomers 35000 / 50000	12274907	7
Caelo	Carbomers 35000 / 50000	11307511	1
Caelo	Carbomers 35000 / 50000	12274908	4
Caelo	Carbomers 35000 / 50000	12274912	5
Caelo	Carbomers 35000 / 50000	11013605	2
Caelo	Carbomers 35000 / 50000	2913M1232	1
Caelo	Carbomers 35000 / 50000	28111310	1
Caelo	Carbomers 35000 / 50000	31631293	1
Caelo	Carbomers 35000 / 50000	13194511	1
Caelo	Carbomers 35000 / 50000	14016208	7
Caelo	Carbomers 35000 / 50000	15015703	1
Caelo	Carbomers 35000 / 50000	15101802	5
Caelo	Carbomers 35000 / 50000	1410001-02	1

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Supplier	Substance	Batch	Spectra
Caelo	Carbomers 35000 / 50000	15101807	3
Caelo	Carbomers 35000 / 50000	1510801	1
Caelo	Carbomers 35000 / 50000	15257403	1
Caelo	Carbomers 35000 / 50000	154390002	1
Caelo	Carbomers 35000 / 50000	1604032-01	1
Caelo	Carbomers 35000 / 50000	16253004	10
Caelo	Carbomers 35000 / 50000	11676321	1
Caelo	Carbomers 35000 / 50000	1081702	1
Caelo	Carbomers 35000 / 50000	17361402	7
Caelo	Carbomers 35000 / 50000	17361403	4
Caelo	Carbomers 35000 / 50000	18092401	21
Caelo	Carbomers 35000 / 50000	1810024-01	1
Caelo	Carbomers 35000 / 50000	18092405	9
Caelo	Carbomers 35000 / 50000	18092406	1
Caelo	Carbomers 35000 / 50000	9011903	1
Caelo	Carbomers 35000 / 50000	18307408	1
Caelo	Carbomers 35000 / 50000	19145601	1
Caelo	Carbomers 35000 / 50000	18307411	1
Caelo	Carbomers 35000 / 50000	18307401	5
Caelo	Carbomers 35000 / 50000	13186203	3
Caelo	Carbomers 35000 / 50000	16253009	9
Caelo	Carbomers 35000 / 50000	14149905	1
Caelo	Carbomers 35000 / 50000	13186201	2
Caelo	Carbomers 35000 / 50000	18307403	4
Caelo	Carbomers 35000 / 50000	1311027-02	1
Caelo	Carbomers 35000 / 50000	16253011	1
Caelo	Carbomers 35000 / 50000	12274922	1
Caelo	Carbomers 35000 / 50000	12274914	3
Caelo	Carbomers 35000 / 50000	13186205	6
Caelo	Carbomers 35000 / 50000	14149910	2
Caelo	Carbomers 35000 / 50000	13194507	4
Caelo	Carbomers 35000 / 50000	2215M-01232	1
Caelo	Carbomers 35000 / 50000	15257401	1
Caelo	Carbomers 35000 / 50000	16253001	1
Caelo	Carbomers 35000 / 50000	12274910	1
Caelo	Carbomers 35000 / 50000	12274916	8
Caelo	Carbomers 35000 / 50000	13194501	5
Caelo	Carbomers 35000 / 50000	13194503	7
Caelo	Carbomers 35000 / 50000	16253007	6
Caelo	Carbomers 35000 / 50000	16253014	3
Caelo	Carbomers 35000 / 50000	192276003	1
Caelo	Carbomers 35000 / 50000	18092411	2
Caelo	Carbomers 35000 / 50000	14149906	3
Caelo	Carbomers 35000 / 50000	1610024-01	1
Caelo	Carbomers 35000 / 50000	17053182	1
Caelo	Carbomers 35000 / 50000	181016184	1
Caelo	Carbomers 35000 / 50000	1706015-01	1
Caelo	Carbomers 35000 / 50000	18049304	1
Caelo	Carbomers 35000 / 50000	180924006	1
Caelo	Carbomers 35000 / 50000	18307413	1
Caelo	Carbomers 35000 / 50000	3441	1
Caelo	Carbomers 35000 / 50000	15439003	11
Caelo	Carbomers 35000 / 50000	19227602	1
Caelo	Carbomers 35000 / 50000	15015702	1
Caelo	Carbomers 35000 / 50000	15101801	5
Caelo	Carbomers 35000 / 50000	15101810	5
Caelo	Carbomers 35000 / 50000	16253005	6
Caelo	Carbomers 35000 / 50000	16253002	1
Caelo	Carbomers 35000 / 50000	18092412	1
Caelo	Carbomers 35000 / 50000	14149911	2

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Supplier	Substance	Batch	Spectra
Caelo	Carbomers 35000 / 50000	11351604	1
Caelo	Carbomers 35000 / 50000	13194505	2
Caelo	Carbomers 35000 / 50000	13194512	1
Caelo	Carbomers 35000 / 50000	14149904	1
Caelo	Carbomers 35000 / 50000	15101809	4
Caelo	Carbomers 35000 / 50000	15439002	9
Caelo	Carbomers 35000 / 50000	16237501	1
Caelo	Carbomers 35000 / 50000	17146501	2
Caelo	Carbomers 35000 / 50000	18092408	5
Caesar & Loretz GmbH	Carbomers 35000 / 50000	18092401	2
Caesar & Loretz GmbH	Carbomers 35000 / 50000	19024501	1
Caesar & Loretz GmbH	Carbomers 35000 / 50000	18307410	1
Caesar & Loretz GmbH	Carbomers 35000 / 50000	18307407	1
Caesar & Loretz GmbH / p...	Carbomers 35000 / 50000	19227601	1
Caesar&Loretz,Phönix,06...	Carbomers 35000 / 50000	15439003	1
EuRho	Carbomers 35000 / 50000	1210037-01	1
EuRho	Carbomers 35000 / 50000	1410001-01	2
Euro	Carbomers 35000 / 50000	1410001-01	2
Euro OTC	Carbomers 35000 / 50000	1512010-02	4
Euro OTC	Carbomers 35000 / 50000	130800601	1
Euro OTC	Carbomers 35000 / 50000	102026590	1
Euro OTC	Carbomers 35000 / 50000	1311027-01	3
Euro OTC	Carbomers 35000 / 50000	1512010-01	7
Euro OTC	Carbomers 35000 / 50000	151210-02	1
Euro OTC	Carbomers 35000 / 50000	1607028-01	7
Euro OTC	Carbomers 35000 / 50000	1610024-01	16
Euro OTC	Carbomers 35000 / 50000	16253002	1
Euro OTC	Carbomers 35000 / 50000	1801044-01	6
Euro OTC	Carbomers 35000 / 50000	12052014A	1
Euro OTC	Carbomers 35000 / 50000	141000-01	1
Euro OTC	Carbomers 35000 / 50000	141000101	1
Euro OTC	Carbomers 35000 / 50000	1604032-01	7
Euro OTC	Carbomers 35000 / 50000	120202001	2
Euro OTC	Carbomers 35000 / 50000	1810019-01	3
Euro OTC	Carbomers 35000 / 50000	1202020-01	2
Euro OTC	Carbomers 35000 / 50000	16253014	1
Euro OTC	Carbomers 35000 / 50000	41 (1810019-01)	1
Euro OTC	Carbomers 35000 / 50000	1903007-01	1
Euro OTC	Carbomers 35000 / 50000	101616773	2
Euro/Gehe	Carbomers 35000 / 50000	1604032-01	1
Euro/Phönix	Carbomers 35000 / 50000	161002401	1
Euro/Sanacorp	Carbomers 35000 / 50000	1305007-01	1
Euro OTC	Carbomers 35000 / 50000	1410001-01	13
Euro OTC	Carbomers 35000 / 50000	1908029-01	1
Euro OTC	Carbomers 35000 / 50000	101217279	1
Euro OTC	Carbomers 35000 / 50000	1702012-01	1
Fagron	Carbomers 35000 / 50000	13194503	1
Fischer/Gehe	Carbomers 35000 / 50000	1410001-02	1
Gatt-Koller	Carbomers 35000 / 50000	1800201	1
Gehe	Carbomers 35000 / 50000	13194505	1
Gehe	Carbomers 35000 / 50000	16237501	1
GEHE	Carbomers 35000 / 50000	18092405	1
Caelo	Carbomers 35000 / 50000	18092402	4
Hepart AG	Carbomers 35000 / 50000	12274916	1
Ichthyol/Phönix	Carbomers 35000 / 50000	14149905	1
Jenne	Carbomers 35000 / 50000	18049301	1
L10/apo-ident	Carbomers 35000 / 50000	1512010-01	1
Fagron	Carbomers 35000 / 50000	1607028-01	1
L30	Carbomers 35000 / 50000	1610024-01	1
L30	Carbomers 35000 / 50000	1801044-01	2

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Supplier	Substance	Batch	Spectra
Noweda	Carbomers 35000 / 50000	16253012	1
Euro OTC	Carbomers 35000 / 50000	1210037-01	6
Euro OTC	Carbomers 35000 / 50000	4311027-01	1
Euro OTC	Carbomers 35000 / 50000	1706015-01	3
Euro OTC	Carbomers 35000 / 50000	1305007-01	2
Phoenix	Carbomers 35000 / 50000	18307402	1
Phoenix	Carbomers 35000 / 50000	19227602	1
Phoenix 16.04.2014	Carbomers 35000 / 50000	13194503	1
Caelo	Carbomers 35000 / 50000	14016209	1
Caelo	Carbomers 35000 / 50000	16253012	5
Rezepturlager - Verläng...	Carbomers 35000 / 50000	115/14	1
Sanacaorp	Carbomers 35000 / 50000	14149905	1
Sanacorp	Carbomers 35000 / 50000	12274922	1
Sanacorp	Carbomers 35000 / 50000	6/AKD13	1
Sanacorp	Carbomers 35000 / 50000	1311027-01	1
Sanacorp	Carbomers 35000 / 50000	14149911	1
Sanacorp	Carbomers 35000 / 50000	1604032-01	1
Sanacorp	Carbomers 35000 / 50000	160702801	1
Caelo	Carbomers 35000 / 50000	11351618	3
Caelo	Carbomers 35000 / 50000	162375	1
Euro OTC	Carbomers 35000 / 50000	1311027-02	7
Caelo	Carbomers 35000 / 50000	13186207	1
Caelo	Carbomers 35000 / 50000	162530	1
Caelo	Carbomers 35000 / 50000	14057902	2
Caelo	Carbomers 35000 / 50000	14057903	2
Euro OTC	Carbomers 35000 / 50000		1
Nachtestung	Carbomers 35000 / 50000		1

- 110 820 spectra from 742 *Apo-Ident* customers from a total of 31 762 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Carbomers 35000 / 50000* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carbomers 35000 / 50000* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	460	0	110 229
Type B	0	480	0	118 662
Type C	0	414	13	110 820

The substance/substance group *Carbomers 35000 / 50000* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.7500 %)
Type C	100.0000 % (> 99.8899 %)	96.9555 % (> 96.2529 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Carbomers 35000 / 50000* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-glutathione	21.72	—
Calcium citrate tetrahydrate	49.30	—
Magnesium citrate	52.79	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Carbomers 35000 / 50000* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22548	22548	0.00	32.33
20978	20978	0.00	31.48
20979	20979	0.00	33.04
21354	22548	3.01	31.14
21557	22548	4.32	30.21
21561	22548	3.19	31.56
22250	22250	0.00	34.30
22686	22686	0.00	31.99
22852	22852	0.00	33.54
22759	22759	0.00	23.29

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20866-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s); Carmellosum natricum (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)

Special notes

When selecting the *Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)	9	2	39

Second-stage model

For differentiation of the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Carmellose sodiu...	12354404	20866	40	1401185
Caelo	Carmellose sodiu...	13104807	20872	40	1401186
Caelo	Carmellose sodiu...	14029211	21382	40	20140127
Caelo	Carmellose sodiu...	13299310	21432	60	20131002
Caelo	Carmellose sodiu...	161714	22645	40	20160713*
Caelo	Carmellose sodiu...	16171406	23187	40	AR-17-FG-015964-01
Caelo	Carmellose sodiu...	180486	24039	40	20180228*
Fagron	Carmellose sodiu...	13D22-N02	20892	40	1401187
Fagron	Carmellose sodiu...	18E15-B04-354617	24868	40	20180620

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 9 reference samples from the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s). These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 309 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 80 spectra of 2 reference samples from the substance/substance group *Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Carmellose sodium (400 / 450...	17062304	23519	40
Caelo	Carmellose sodium (400 / 450...	172446	23623	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 73 spectra from 39 *Apo-Ident* customers from 42 batches from the substance/substance group *Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s)*.
- Among them are spectra of independent samples from 39 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Carmellose sodium (400 / 450...	13104813	1
Caelo	Carmellose sodium (400 / 450...	13104802	3
Caelo	Carmellose sodium (400 / 450...	12255708	1
Caelo	Carmellose sodium (400 / 450...	12354414	1
Caelo	Carmellose sodium (400 / 450...	28051402	1
Caelo	Carmellose sodium (400 / 450...	14149806	1
Caelo	Carmellose sodium (400 / 450...	14029201	1
Caelo	Carmellose sodium (400 / 450...	15123909	1
Caelo	Carmellose sodium (400 / 450...	17062304	4
Caelo	Carmellose sodium (400 / 450...	17052304	1
Caelo	Carmellose sodium (400 / 450...	17062303	1
Caelo	Carmellose sodium (400 / 450...	17062307	3
Caelo	Carmellose sodium (400 / 450...	17062309	3
Caelo	Carmellose sodium (400 / 450...	25041805	1
Caelo	Carmellose sodium (400 / 450...	12354408	1
Caelo	Carmellose sodium (400 / 450...	13104813	2
Caelo	Carmellose sodium (400 / 450...	13G19-N02	1
Caelo	Carmellose sodium (400 / 450...	15123908	3
Caelo	Carmellose sodium (400 / 450...	1315Q-03302	1
Caelo	Carmellose sodium (400 / 450...	17348606	1
Caelo	Carmellose sodium (400 / 450...	17244601	1
Caelo	Carmellose sodium (400 / 450...	11124211	1
Caelo	Carmellose sodium (400 / 450...	13299302	2
Caelo	Carmellose sodium (400 / 450...	15123901	3
Caelo	Carmellose sodium (400 / 450...	15123912	1
Caelo	Carmellose sodium (400 / 450...	17348605	1
Caesar & Loretz GmbH	Carmellose sodium (400 / 450...	17062307	1
Caesar & Loretz GmbH/Kr...	Carmellose sodium (400 / 450...	18048604	1

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Supplier	Substance	Batch	Spectra
Fagro	Carmellose sodium (400 / 450...	15G03-B02-321790	1
Fagro	Carmellose sodium (400 / 450...	16G05-B05-329314	1
Fagro	Carmellose sodium (400 / 450...	17C20-B07-337104	1
Fagro	Carmellose sodium (400 / 450...	17K06-B03-345975	1
Fagron	Carmellose sodium (400 / 450...	15G03-Bo2-312862	1
Gehe	Carmellose sodium (400 / 450...	17062307	1
GEHE	Carmellose sodium (400 / 450...	17062307	1
Caelo	Carmellose sodium (400 / 450...	13104810	3
Gehe 06.10.14	Carmellose sodium (400 / 450...	13299312	1
Gutenberg-Apotheke	Carmellose sodium (400 / 450...	4811E-03302	1
Caelo	Carmellose sodium (400 / 450...	16171402	3
Noweda	Carmellose sodium (400 / 450...	12354401	1
Phoenix	Carmellose sodium (400 / 450...	17348601	2
Caelo	Carmellose sodium (400 / 450...	12354416	3
Sanacorp	Carmellose sodium (400 / 450...	AKD6	1
Caelo	Carmellose sodium (400 / 450...	17348601	4
Caelo	Carmellose sodium (400 / 450...	13104807	2
Caelo	Carmellose sodium (400 / 450...	14029211	1
Fagron	Carmellose sodium (400 / 450...	13D22-N02	1

- 111 174 spectra from 742 *Apo-Ident* customers from a total of 31 852 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	380	0	110 309
Type B	0	78	2	119 062
Type C	0	72	1	111 174

The substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.9893 %)	97.5000 % (> 93.7500 %)
Type C	100.0000 % (> 99.8899 %)	98.6301 % (> 94.5205 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	33.06	—
Hyaluronic acid sodium salt	34.20	—
SyrSpend [®] SF Alka	37.99	—
Trometamol	48.17	—
Heparin sodium	51.20	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Carmellose sodium* (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20872	20872	0.00	40.41
21382	20872	6.74	37.03
20892	20892	0.00	45.67
24868	20892	13.87	42.17
22645	22645	0.00	36.08
20866	20866	0.00	42.48
21432	20866	7.55	46.30
23187	23187	0.00	47.76
24039	24039	0.00	33.06

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Cellulose, microcrystalline
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20708-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cellulose, microcrystalline; Cellulosum microcristallinum

Special notes

When selecting the *Cellulose, microcrystalline* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cellulose, microcrystalline	6	6	33

Second-stage model

For differentiation of the substance/substance group *Cellulose, microcrystalline* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cellulose, microcrystalline*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Cellulose, micro...	1201004-01	20728	40	20120201
Euro OTC	Cellulose, micro...	1211037-01	21080	30	20121207
Euro OTC	Cellulose, micro...	1211037-01	21085	40	20121207
Euro OTC	Cellulose, micro...	1507022	21857	60	20150805*
Euro OTC	Cellulose, micro...	1604029	22559	40	20160512*
Fagron	Cellulose, micro...	12C23-N06	20708	70	1403080
Fagron	Cellulose, micro...	16B24-B11-323324	22896	40	20160311

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Cellulose, microcrystalline*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 369 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Cellulose, microcrystalline*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Cellulose, microcrystalline	1607042	22794	40
Euro OTC	Cellulose, microcrystalline	1604029-01	22815	40
Euro OTC	Cellulose, microcrystalline	1610030	22876	40
Euro OTC	Cellulose, microcrystalline	1712009	23909	40
Euro OTC	Cellulose, microcrystalline	1811011	24346	40
Euro OTC	Cellulose, microcrystalline	1911018	25076	40

- 118902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 67 spectra from 42 *Apo-Ident* customers from 34 batches from the substance/substance group *Cellulose, microcrystalline*.
- Among them are spectra of independent samples from 33 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
apo-ident.	Cellulose, microcrystalline	1604029-01	1
Caelo	Cellulose, microcrystalline	8722	1
Caelo	Cellulose, microcrystalline	1610030-01	4
Caelo	Cellulose, microcrystalline	160402901	1
EuRho	Cellulose, microcrystalline	1201004-02	1
Euro OTC	Cellulose, microcrystalline	121103701	1
Euro OTC	Cellulose, microcrystalline	8710	1
Euro OTC	Cellulose, microcrystalline	2763	1
Euro OTC	Cellulose, microcrystalline	2780	1
Euro OTC	Cellulose, microcrystalline	1607042-01	3
Euro OTC	Cellulose, microcrystalline	1610030-01	3
Euro OTC	Cellulose, microcrystalline	1712009-01	1
Euro OTC	Cellulose, microcrystalline	1811011-01	3
Euro OTC	Cellulose, microcrystalline	1604029-01	8
Euro OTC	Cellulose, microcrystalline	150702201	1
Euro OTC	Cellulose, microcrystalline	1309001-01	3
Euro OTC	Cellulose, microcrystalline	1201004-02	2
Euro OTC	Cellulose, microcrystalline	135010001	1
Euro OTC	Cellulose, microcrystalline	1712009-02	3
Euro OTC	Cellulose, microcrystalline	150722-01	1
Euro OTC	Cellulose, microcrystalline	160704201	1
Euro/Noweda	Cellulose, microcrystalline	1410002-02	1
Euro OTC	Cellulose, microcrystalline	700204	1
Euro OTC	Cellulose, microcrystalline	1410002-01	4
Euro OTC	Cellulose, microcrystalline	1309001-02	3
Fagron	Cellulose, microcrystalline	13A03-N01	1
Fagron	Cellulose, microcrystalline	15C03-B06-305242	1

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Supplier	Substance	Batch	Spectra
Fagron	Cellulose, microcrystalline	17A11-B04-331463	1
Fagron	Cellulose, microcrystalline	17A11-B04-340541	1
Fagron	Cellulose, microcrystalline	9K10-N10	1
Fagron	Cellulose, microcrystalline	17/04-B50	1
Fagron	Cellulose, microcrystalline	2013M-01350	1
Fagron	Cellulose, microcrystalline	17I04-B50-351755	1
Fagron	Cellulose, microcrystalline	18/19-B50-360110	1
Koisser	Cellulose, microcrystalline	E0790	1
Phnoix	Cellulose, microcrystalline	1211037-01	1
Phoenix	Cellulose, microcrystalline	1309001-02	1
Phoenix	Cellulose, microcrystalline	3235	1
Phoenix	Cellulose, microcrystalline	1712009-02	1
Euro OTC	Cellulose, microcrystalline	1211037-01	2

- 111 180 spectra from 742 *Apo-Ident* customers from a total of 31 857 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cellulose, microcrystalline* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cellulose, microcrystalline* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	240	0	118 902
Type C	0	67	0	111 180

The substance/substance group *Cellulose, microcrystalline* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 91.0448 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cellulose, microcrystalline* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rice starch	34.51	—
SyrSpend® SF Alka	38.13	—
Hyaluronic acid sodium salt	58.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cellulose, microcrystalline* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20708	20708	0.00	47.56
20728	20708	3.22	48.00
21080	20708	3.43	46.89
21085	20708	3.43	46.77
21857	21857	0.00	49.82
22896	21857	2.19	48.04
22559	22559	0.00	53.98

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Cetostearyl alcohol
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20738-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cetostearyl alcohol; Alcohol cetylicus; Alcohol cetylicus et stearylicus; Alcohol cetylicus et stearylicus emulsificans A; Cetomacrogol emulsifying wax 1000 NI; Cetyl alcohol; Emulsifying cetostearyl alcohol (type A)

Special notes

When selecting the *Cetostearyl alcohol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cetomacrogol emulsifying wax 1000 NI	4	1	10
Cetostearyl alcohol	3	3	111
Cetyl alcohol	5	2	45
Emulsifying cetostearyl alcohol (type A)	8	7	163

Second-stage model

For differentiation of the substance/substance group *Cetostearyl alcohol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cetostearyl alcohol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Cetomacrogol emu...	14055001	21381	40	20140225
Caelo	Cetomacrogol emu...	15277504	22390	40	20150828
Fagron	Cetomacrogol emu...	12H07-N06	20738	40	20120905
Fagron	Cetomacrogol emu...	13C05-B40-289262	21054	40	1408003
Caelo	Cetostearyl alco...	14054504	21314	40	20140226
Caelo	Cetostearyl alco...	14054504	21442	60	20140226
Caelo	Cetostearyl alco...	17049205	23725	40	20170302
Fagron	Cetostearyl alco...	13C13-N13	20968	40	1402265
Caelo	Cetyl alcohol	13096901	20896	40	1405179
Caelo	Cetyl alcohol	13286502	21318	40	20130925
Caelo	Cetyl alcohol	13286502	21435	60	20130925
Caelo	Cetyl alcohol	15323301	22266	60	AR-16-FG-008835-01
Caelo	Cetyl alcohol	161063	22398	40	20160420*
Caelo	Cetyl alcohol	161063	22399	40	20160420*
Caelo	Cetyl alcohol	161063	22400	40	20160420*
Caelo	Cetyl alcohol	161063	22401	40	20160420*
Caelo	Cetyl alcohol	161063	22402	40	20160420*
Caelo	Cetyl alcohol	161063	22403	40	20160420*
Euro OTC	Cetyl alcohol	1508014-01	22611	40	20150821
Caelo	Emulsifying ceto...	13233005	21319	30	1506057
Caelo	Emulsifying ceto...	13233005	21434	60	20130816
Caelo	Emulsifying ceto...	14322505	21830	60	20141031
Caelo	Emulsifying ceto...	153857	22331	60	20151202*
Caelo	Emulsifying ceto...	153857	22332	60	20151202*
Caelo	Emulsifying ceto...	153856	22333	60	20160210*
Caelo	Emulsifying ceto...	153856	22334	60	20160210*
Euro OTC	Emulsifying ceto...	1510043	21998	60	20151124*
Euro OTC	Emulsifying ceto...	1504010-01	22264	60	20150423
Fagron	Emulsifying ceto...	13L17-B05	21279	40	1505070
Fagron	Emulsifying ceto...	16I13-B01-326511	23022	40	20161024

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 1410 spectra of 30 reference samples from the substance/substance group *Cetostearyl alcohol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 20 different batches.
- 109 279 spectra from a total of 1946 batches from further 387 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 640 spectra of 16 reference samples from the substance/substance group *Cetostearyl alcohol*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Cetomacrogol emulsifying wax...	160804	22395	40
Caelo	Cetostearyl alcohol	170492	23097	40
Caelo	Cetostearyl alcohol	172979	23819	40
Caelo	Cetostearyl alcohol	190552	24721	40
Caelo	Cetyl alcohol	170473	23068	40
Caelo	Cetyl alcohol	173155	23973	40
Caelo	Emulsifying cetostearyl alco...	171980	23575	40
Caelo	Emulsifying cetostearyl alco...	180180	24033	40
Caelo	Emulsifying cetostearyl alco...	191857	25068	40
Euro OTC	Emulsifying cetostearyl alco...	1604013	22540	40
Euro OTC	Emulsifying cetostearyl alco...	1701031	22999	40
Euro OTC	Emulsifying cetostearyl alco...	1705001	23381	40
Euro OTC	Emulsifying cetostearyl alco...	1711001	23737	40
Caelo	Cetomacrogol emulsifying wax...	160804	22396	40
Caelo	Cetomacrogol emulsifying wax...	160804	22397	40
Euro OTC	Emulsifying cetostearyl alco...	1711001	25093	40

- 118 502 spectra from a total of 2407 batches from further 796 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 849 spectra from 316 *Apo-Ident* customers from 280 batches from the substance/substance group *Cetostearyl alcohol*.
- Among them are spectra of independent samples from 267 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Cetomacrogol emulsifying wax...	8073743	1
Caelo	Cetomacrogol emulsifying wax...	15113703	1
Caelo	Cetomacrogol emulsifying wax...	15277501	1
Caelo	Cetomacrogol emulsifying wax...	15277505	1
Caelo	Cetomacrogol emulsifying wax...	16080407	1
Caelo	Cetomacrogol emulsifying wax...	16348101	1
Caelo	Cetomacrogol emulsifying wax...	16080403	1
Caelo	Cetomacrogol emulsifying wax...	14055002	1
Caelo	Cetomacrogol emulsifying wax...	18291406	1
Phoenix	Cetomacrogol emulsifying wax...	18335402	1
ahd/lamotte	Cetostearyl alcohol	13210504	1
Caelo	Cetostearyl alcohol	14054508	3
Caelo	Cetostearyl alcohol	11162305	1
Caelo	Cetostearyl alcohol	12021304	1
Caelo	Cetostearyl alcohol	14061317	1
Caelo	Cetostearyl alcohol	13018305	4
Caelo	Cetostearyl alcohol	1314405	1
Caelo	Cetostearyl alcohol	13206206	3
Caelo	Cetostearyl alcohol	14215007	6
Caelo	Cetostearyl alcohol	8041708	1
Caelo	Cetostearyl alcohol	160914	1
Caelo	Cetostearyl alcohol	16048812	2
Caelo	Cetostearyl alcohol	16230603	2
Caelo	Cetostearyl alcohol	13-B01-327355	1
Caelo	Cetostearyl alcohol	1705001-01	1
Caelo	Cetostearyl alcohol	17049209	2
Caelo	Cetostearyl alcohol	18248502	5
Caelo	Cetostearyl alcohol	17321603	12
Caelo	Cetostearyl alcohol	18A23-B04	1
Caelo	Cetostearyl alcohol	18248510	1
Caelo	Cetostearyl alcohol	171215CSA/15272717	1
Caelo	Cetostearyl alcohol	11302101	1
Caelo	Cetostearyl alcohol	17321303	6
Caelo	Cetostearyl alcohol	15272702	1
Caelo	Cetostearyl alcohol	13018306	1
Caelo	Cetostearyl alcohol	15272717	5
Caelo	Cetostearyl alcohol	14346202	1
Caelo	Cetostearyl alcohol	17D28-B06-334609	1
Caelo	Cetostearyl alcohol	12025301	2
Caelo	Cetostearyl alcohol	14346201	3
Caelo	Cetostearyl alcohol	15272709	6
Caelo	Cetostearyl alcohol	17321305	1
Caesar & Loretz GmbH	Cetostearyl alcohol	17056806	1
Caesar & Loretz GmbH, 4...	Cetostearyl alcohol	11302101	1
Caesar/Noweda	Cetostearyl alcohol	2911E-01077	2
Caesar/Noweda	Cetostearyl alcohol	15272705	1
Cealo	Cetostearyl alcohol	19012504	1
Cealo/Alliance Healthcare	Cetostearyl alcohol	18291403	1
Ebert-Jacobi	Cetostearyl alcohol	16230603	1
Euro OTC	Cetostearyl alcohol	20270912-2	1
Euro OTC	Cetostearyl alcohol	2806	1
Euro OTC	Cetostearyl alcohol	150401001	1
Euro OTC	Cetostearyl alcohol	17050001-01	1
Euro OTC	Cetostearyl alcohol	1204015-01	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Cetostearyl alcohol	1107035-01	1
Fagron	Cetostearyl alcohol	11f30-n11	1
Fagron	Cetostearyl alcohol	12g02-n04	1
Fagron	Cetostearyl alcohol	10F17-N02	1
Fagron	Cetostearyl alcohol	11E17-N13	1
Fagron	Cetostearyl alcohol	12E30-N13	1
Fagron	Cetostearyl alcohol	12J17-N05	2
Fagron	Cetostearyl alcohol	12/17-N05	1
Fagron	Cetostearyl alcohol	12K22-N03	3
Fagron	Cetostearyl alcohol	14346201	1
Fagron	Cetostearyl alcohol	17F21-B01	1
Fagron	Cetostearyl alcohol	18A23-B04	1
Fagron	Cetostearyl alcohol	14G31-B03-297611	1
Fagron	Cetostearyl alcohol	7886542	1
Fagron	Cetostearyl alcohol	3414E-01078	1
Gatt-Koller	Cetostearyl alcohol	1803965	1
Gehe	Cetostearyl alcohol	15272717	1
Gehe	Cetostearyl alcohol	15272713	1
Herba	Cetostearyl alcohol	KNC1133J18	1
Noweda	Cetostearyl alcohol	12065709	1
Phoenix	Cetostearyl alcohol	14322505	1
Phoenix	Cetostearyl alcohol	3071	1
Phoenix	Cetostearyl alcohol	18A23-B04-352987	1
Phönix	Cetostearyl alcohol	17D28-B06-338141	1
Sanacorp	Cetostearyl alcohol	575778	1
Sanacorp	Cetostearyl alcohol	13206206	1
Fagron	Cetostearyl alcohol	12J17-N05	1
AHD	Cetyl alcohol	17321603	1
Caelo	Cetyl alcohol	12018605	2
Caelo	Cetyl alcohol	11320702	2
Caelo	Cetyl alcohol	11153405	1
Caelo	Cetyl alcohol	20250112-1	1
Caelo	Cetyl alcohol	12271103	5
Caelo	Cetyl alcohol	12338604	6
Caelo	Cetyl alcohol	1212E-01076	1
Caelo	Cetyl alcohol	1112013B	1
Caelo	Cetyl alcohol	13096904	2
Caelo	Cetyl alcohol	14262204	5
Caelo	Cetyl alcohol	1523316	1
Caelo	Cetyl alcohol	16335807	7
Caelo	Cetyl alcohol	17047307	8
Caelo	Cetyl alcohol	28101701	1
Caelo	Cetyl alcohol	17047303	1
Caelo	Cetyl alcohol	17234902	1
Caelo	Cetyl alcohol	17234903	1
Caelo	Cetyl alcohol	7071807	1
Caelo	Cetyl alcohol	17234904	1
Caelo	Cetyl alcohol	18237701	5
Caelo	Cetyl alcohol	19012509	1
Caelo	Cetyl alcohol	14349101	14
Caelo	Cetyl alcohol	13210504	9
Caelo	Cetyl alcohol	16106307	4
Caelo	Cetyl alcohol	19012504	1
Caelo	Cetyl alcohol	15323311	10
Caelo	Cetyl alcohol	15323316	3
Caelo	Cetyl alcohol	17321612	6
Caelo	Cetyl alcohol	18153102	8
Caesar & Loretz GmbH	Cetyl alcohol	18153102	1
Caesar & Loretz/Gehe	Cetyl alcohol	19012504	1
EuRho	Cetyl alcohol	1206020-01	1

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Supplier	Substance	Batch	Spectra
EuRho Anzag ek:3,47EUR	Cetyl alcohol	110505501	1
Euro OTC	Cetyl alcohol	150818C	1
Euro OTC	Cetyl alcohol	1105055-01	1
Euro OTC	Cetyl alcohol	1206020-01	1
Euro OTC	Cetyl alcohol	1211002-01	2
Fagron	Cetyl alcohol	12A-02N12	1
Fagron	Cetyl alcohol	17321612	1
Finze	Cetyl alcohol	10321703	1
Gatt-Koller	Cetyl alcohol	1690/06162416	1
Gehe	Cetyl alcohol	19012504	1
Kehr	Cetyl alcohol	17047303	1
Caelo	Cetyl alcohol	16335802	7
Phoenix 10.01.2020	Cetyl alcohol	19012509	1
Caelo	Cetyl alcohol	15323308	1
Caelo	Cetyl alcohol	16335805	1
Phonix	Cetyl alcohol	13210504	1
Phönix	Cetyl alcohol	13096901	1
Caelo	Cetyl alcohol	17047306	3
Sanacorpaelo /Sanacorp	Cetyl alcohol	1AKS11	1
A.H.D.	Emulsifying cetostearyl alco...	12L19-N03	2
ALH	Emulsifying cetostearyl alco...	15271405	1
Alliance Health 24.07.2...	Emulsifying cetostearyl alco...	13L17-B05-289805	1
alliance health. 05.05...	Emulsifying cetostearyl alco...	14G31-B03-297610	1
Anzag	Emulsifying cetostearyl alco...	12G02-N04	1
Fagron	Emulsifying cetostearyl alco...	12G02N04	1
Audor Pharma	Emulsifying cetostearyl alco...	16238602	1
Bombastus	Emulsifying cetostearyl alco...	308514	3
Bombastus	Emulsifying cetostearyl alco...	288691	3
Bombastus	Emulsifying cetostearyl alco...	295148	2
Bombastus	Emulsifying cetostearyl alco...	303935	1
Bombastus	Emulsifying cetostearyl alco...	18003437	4
Bombastus	Emulsifying cetostearyl alco...	300132	5
Bombastus	Emulsifying cetostearyl alco...	19002555	3
Bombastus	Emulsifying cetostearyl alco...	18002312	3
Bombastus	Emulsifying cetostearyl alco...	265360	1
Bombastus	Emulsifying cetostearyl alco...	278418	1
Bombastus	Emulsifying cetostearyl alco...	18003404	1
Caelo	Emulsifying cetostearyl alco...	25051201	1
Caelo	Emulsifying cetostearyl alco...	18081201	1
Caelo	Emulsifying cetostearyl alco...	12065709	7
Caelo	Emulsifying cetostearyl alco...	12229402	2
Caelo	Emulsifying cetostearyl alco...	11291103	1
Caelo	Emulsifying cetostearyl alco...	13144104	2
Caelo	Emulsifying cetostearyl alco...	24101305	1
Caelo	Emulsifying cetostearyl alco...	13144105	12
Caelo	Emulsifying cetostearyl alco...	13233001	1
Caelo	Emulsifying cetostearyl alco...	2011404	1
Caelo	Emulsifying cetostearyl alco...	23091402	1
Caelo	Emulsifying cetostearyl alco...	14G31-B03-305612	3
Caelo	Emulsifying cetostearyl alco...	13233008	2
Caelo	Emulsifying cetostearyl alco...	14158202	1
Caelo	Emulsifying cetostearyl alco...	5011505	1
Caelo	Emulsifying cetostearyl alco...	14322502	2
Caelo	Emulsifying cetostearyl alco...	13233006	1
Caelo	Emulsifying cetostearyl alco...	31032015B	1
Caelo	Emulsifying cetostearyl alco...	23051503	1
Caelo	Emulsifying cetostearyl alco...	15090703	2
Caelo	Emulsifying cetostearyl alco...	15271405	10
Caelo	Emulsifying cetostearyl alco...	15271403	9
Caelo	Emulsifying cetostearyl alco...	15271402	9

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Supplier	Substance	Batch	Spectra
Caelo	Emulsifying cetostearyl alco...	15385606	1
Caelo	Emulsifying cetostearyl alco...	13144103	1
Caelo	Emulsifying cetostearyl alco...	15271408	3
Caelo	Emulsifying cetostearyl alco...	16119604	12
Caelo	Emulsifying cetostearyl alco...	608/10072017	1
Caelo	Emulsifying cetostearyl alco...	15071704	1
Caelo	Emulsifying cetostearyl alco...	9170717	1
Caelo	Emulsifying cetostearyl alco...	17198003	19
Caelo	Emulsifying cetostearyl alco...	17198002	4
Caelo	Emulsifying cetostearyl alco...	29091803	1
Caelo	Emulsifying cetostearyl alco...	308514	1
Caelo	Emulsifying cetostearyl alco...	18018001	2
Caelo	Emulsifying cetostearyl alco...	18291404	3
Caelo	Emulsifying cetostearyl alco...	11291101	1
Caelo	Emulsifying cetostearyl alco...	12331407	3
Caelo	Emulsifying cetostearyl alco...	Unbekannt	1
Caelo	Emulsifying cetostearyl alco...	18018005	5
Caelo	Emulsifying cetostearyl alco...	13233002	3
Caelo	Emulsifying cetostearyl alco...	13352102	1
Caelo	Emulsifying cetostearyl alco...	16I13-B01-327864	1
Caelo	Emulsifying cetostearyl alco...	15090701	10
Caelo	Emulsifying cetostearyl alco...	18018006	1
Caelo	Emulsifying cetostearyl alco...	14158201	11
Caelo	Emulsifying cetostearyl alco...	303935	1
Caelo	Emulsifying cetostearyl alco...	3256	1
Caelo	Emulsifying cetostearyl alco...	18291407	2
Caelo	Emulsifying cetostearyl alco...	16119607	2
Caelo	Emulsifying cetostearyl alco...	16238607	10
Caelo	Emulsifying cetostearyl alco...	19185703	1
Caelo	Emulsifying cetostearyl alco...	17261702	3
Caelo	Emulsifying cetostearyl alco...	191857002	1
Caelo	Emulsifying cetostearyl alco...	13L17-B05-289806	1
Caelo	Emulsifying cetostearyl alco...	15271410	1
Caelo	Emulsifying cetostearyl alco...	17056802	1
Caelo	Emulsifying cetostearyl alco...	13144107	2
Caelo	Emulsifying cetostearyl alco...	15385602	3
Caelo	Emulsifying cetostearyl alco...	14322506	2
Caelo	Emulsifying cetostearyl alco...	12134203	1
Caelo	Emulsifying cetostearyl alco...	19032014B	1
Caelo	Emulsifying cetostearyl alco...	15271407	7
Caelo	Emulsifying cetostearyl alco...	17261701	1
Caelo	Emulsifying cetostearyl alco...	19185702	8
Caelo	Emulsifying cetostearyl alco...	11009204	1
Caelo	Emulsifying cetostearyl alco...	12231402	1
Caelo	Emulsifying cetostearyl alco...	18003404	10
Caelo	Emulsifying cetostearyl alco...	14156201	1
Caelo	Emulsifying cetostearyl alco...	14322512	1
Caelo	Emulsifying cetostearyl alco...	15C31-B99-307062	1
Caelo	Emulsifying cetostearyl alco...	15789271	1
Caelo	Emulsifying cetostearyl alco...	17139201	5
Caelo	Emulsifying cetostearyl alco...	12331402	6
Caelo	Emulsifying cetostearyl alco...	16238604	3
Caeolo	Emulsifying cetostearyl alco...	17056807	1
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	13233008	1
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	16119604	3
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	17132001	1
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	18018005	1
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	18248502	2
Caesar & Loretz GmbH	Emulsifying cetostearyl alco...	18291403	1
Caesar &Loretz GmbH	Emulsifying cetostearyl alco...	12065703	1

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Supplier	Substance	Batch	Spectra
Caesar&lorenz,Phoenix	Emulsifying cetostearyl alco...	14158201	1
Caesar&Loretz/Noweda	Emulsifying cetostearyl alco...	15271405	1
Caesar/Lorenz	Emulsifying cetostearyl alco...	13233005	1
Caesar/Noweda	Emulsifying cetostearyl alco...	11343405	1
Caesar/Noweda	Emulsifying cetostearyl alco...	12065707	1
Euro OTC	Emulsifying cetostearyl alco...	1404019-01	2
Euro OTC	Emulsifying cetostearyl alco...	15271403	2
Euro OTC	Emulsifying cetostearyl alco...	150410-01	1
Euro OTC	Emulsifying cetostearyl alco...	1305035-01	2
Euro OTC	Emulsifying cetostearyl alco...	1404019-03	1
Euro OTC	Emulsifying cetostearyl alco...	1604013-02	5
Euro OTC	Emulsifying cetostearyl alco...	10836573	1
Euro OTC	Emulsifying cetostearyl alco...	1705001-01	7
Euro OTC	Emulsifying cetostearyl alco...	1510043-01	3
Euro OTC	Emulsifying cetostearyl alco...	1212019-01	1
Euro OTC	Emulsifying cetostearyl alco...	171001-02	1
Euro OTC	Emulsifying cetostearyl alco...	14G31-B03-297610	1
Euro/Gehe	Emulsifying cetostearyl alco...	150401-01	1
Euroh/Noweda	Emulsifying cetostearyl alco...	1504010-01	1
Euro OTC	Emulsifying cetostearyl alco...	1404019-02	2
Euro OTC	Emulsifying cetostearyl alco...	1711001-02	4
Fagro	Emulsifying cetostearyl alco...	5211Q-01078	1
Fagron	Emulsifying cetostearyl alco...	12G02-N04	12
Fagron	Emulsifying cetostearyl alco...	12C30-N01	2
Fagron	Emulsifying cetostearyl alco...	20260712-2	1
Fagron	Emulsifying cetostearyl alco...	8256792	4
Fagron	Emulsifying cetostearyl alco...	13L17-B05-289805	7
Fagron	Emulsifying cetostearyl alco...	11499002	1
Fagron	Emulsifying cetostearyl alco...	14G31-B03-297610	2
Fagron	Emulsifying cetostearyl alco...	14G31-B03-305612	4
Fagron	Emulsifying cetostearyl alco...	15D24-B02-311993	9
Fagron	Emulsifying cetostearyl alco...	2797	1
Fagron	Emulsifying cetostearyl alco...	16B23-B07-320384	6
Fagron	Emulsifying cetostearyl alco...	161006CSA	1
Fagron	Emulsifying cetostearyl alco...	16B23-B07-323025	3
Fagron	Emulsifying cetostearyl alco...	16B23-B07	1
Fagron	Emulsifying cetostearyl alco...	15789271	1
Fagron	Emulsifying cetostearyl alco...	16I13-B01	2
Fagron	Emulsifying cetostearyl alco...	17D28-B06	1
Fagron	Emulsifying cetostearyl alco...	17D28-B06-338141	6
Fagron	Emulsifying cetostearyl alco...	16990201	1
Fagron	Emulsifying cetostearyl alco...	17F21-B01-344775	2
Fagron	Emulsifying cetostearyl alco...	18A23-B04-352987	2
Fagron	Emulsifying cetostearyl alco...	18A23-B04-355659	1
Fagron	Emulsifying cetostearyl alco...	17894959	1
Fagron	Emulsifying cetostearyl alco...	16I13-B01_326511	1
Fagron	Emulsifying cetostearyl alco...	15D24-B02-308261	5
Fagron	Emulsifying cetostearyl alco...	13L17-B05-294999	4
Fagron	Emulsifying cetostearyl alco...	17028-B06-334609	1
Fagron	Emulsifying cetostearyl alco...	15C31-B00-307062	1
Fagron	Emulsifying cetostearyl alco...	16B23-B07-318218	4
Fagron	Emulsifying cetostearyl alco...	16/13-B01-327355	2
Fagron	Emulsifying cetostearyl alco...	17F21-B01-341021	8
Fagron	Emulsifying cetostearyl alco...	13I06-N04	1
Fagron	Emulsifying cetostearyl alco...	13F07-N05	9
Fagron	Emulsifying cetostearyl alco...	15D24-B02	2
Fagron	Emulsifying cetostearyl alco...	16/13-Bo1-327864	1
Fagron	Emulsifying cetostearyl alco...	12J29-N04	4
Fagron	Emulsifying cetostearyl alco...	13L17B05289805	1
Fagron	Emulsifying cetostearyl alco...	11L22-N09	1

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Supplier	Substance	Batch	Spectra
Fagron	Emulsifying cetostearyl alco...	14G31-B03	1
Fagron	Emulsifying cetostearyl alco...	17D28-B06-334609	4
Fagron	Emulsifying cetostearyl alco...	15C31-B99-307062	5
Fagron	Emulsifying cetostearyl alco...	171216CAE/0016830715	1
Fagron	Emulsifying cetostearyl alco...	17D21-B01-341021	1
Fagron	Emulsifying cetostearyl alco...	18A23-B04-349155	3
Fagron	Emulsifying cetostearyl alco...	12L19-N03	8
Fagron	Emulsifying cetostearyl alco...	13L17-B05-289806	5
Fagron	Emulsifying cetostearyl alco...	3013M-01078	1
Fagron	Emulsifying cetostearyl alco...	2215I-01078	1
Fagron	Emulsifying cetostearyl alco...	9652865	2
Fagron	Emulsifying cetostearyl alco...	18003401	1
fragron	Emulsifying cetostearyl alco...	16113-b01-326511	1
Gehe	Emulsifying cetostearyl alco...	12L19-N03	1
Gehe	Emulsifying cetostearyl alco...	1701031-01	1
Gehe	Emulsifying cetostearyl alco...	18291406	1
Fagron	Emulsifying cetostearyl alco...	12602-N04	1
Caelo	Emulsifying cetostearyl alco...	15090706	3
Henry Lamotte / Noweda	Emulsifying cetostearyl alco...	300132	1
Kehr	Emulsifying cetostearyl alco...	18003404	1
Klenk	Emulsifying cetostearyl alco...	16238607	1
Krieger	Emulsifying cetostearyl alco...	1711001-01	1
L12	Emulsifying cetostearyl alco...	17056806	1
Noweda	Emulsifying cetostearyl alco...	13144104	1
Noweda	Emulsifying cetostearyl alco...	13065576	1
Caelo	Emulsifying cetostearyl alco...	17056806	4
Caelo	Emulsifying cetostearyl alco...	17132001	7
Caelo	Emulsifying cetostearyl alco...	18003401	1
Phoenix	Emulsifying cetostearyl alco...	15789271	1
Phoenix	Emulsifying cetostearyl alco...	17198003	1
Phoenix	Emulsifying cetostearyl alco...	17D28-B06-338141	1
Phoenix 26.11.12	Emulsifying cetostearyl alco...	13144105	1
PHOENIX am07.04.2014	Emulsifying cetostearyl alco...	13F07-N05	1
Phönix	Emulsifying cetostearyl alco...	1323305	1
Phönix	Emulsifying cetostearyl alco...	15C31-B99-307062	1
Phönix	Emulsifying cetostearyl alco...	18A23-B04-355659	1
Euro OTC	Emulsifying cetostearyl alco...	1701031-01	3
Sanacorp	Emulsifying cetostearyl alco...	12J29-N04	1
Sanacorp	Emulsifying cetostearyl alco...	13F07-N05	4
Sanacorp	Emulsifying cetostearyl alco...	13I06-N04	1
Sanacorp	Emulsifying cetostearyl alco...	15090701	1
Caelo	Emulsifying cetostearyl alco...	12C30-N01	1
Caelo	Emulsifying cetostearyl alco...	25/AKD1	1
Taoasis	Emulsifying cetostearyl alco...	303935	2
Caelo	Cetomacrogol emulsifying wax...		2
Caelo	Cetostearyl alcohol	14054504	4
Caelo	Cetostearyl alcohol	14322505	11
Euro OTC	Cetostearyl alcohol	1504010-01	3
Fagron	Cetostearyl alcohol	13L17-B05	2
Fagron	Cetostearyl alcohol	13C13-N13	1
Caelo	Cetyl alcohol	15323301	7
Caelo	Cetyl alcohol	13096901	5
Caelo	Cetyl alcohol	13286502	5
Euro OTC	Cetyl alcohol	1508014-01	1
Caelo	Emulsifying cetostearyl alco...	13233005	12

- 110 398 spectra from 742 *Apo-Ident* customers from a total of 31 614 batches from a further 703 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are docu-

mented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cetostearyl alcohol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cetostearyl alcohol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	1410	0	109 279
Type B	0	636	4	118 502
Type C	0	846	3	110 398

The substance/substance group *Cetostearyl alcohol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.5745 %)
Type B	100.0000 % (> 99.9893 %)	99.3750 % (> 98.9063 %)
Type C	100.0000 % (> 99.8899 %)	99.6466 % (> 99.2933 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cetostearyl alcohol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Non-ionic emulsifying alcohol	17.85	—
Menthol	45.53	—
Glycerol monostearate 40-55%	47.82	—
Glycerol monostearate 60	49.28	—
Glycerol monostearate, emulsifying	50.92	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cetostearyl alcohol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20738	21054	3.71	33.19
22611	22401	17.45	39.59
22390	21054	4.60	41.61
21054	21054	0.00	29.88
21279	21279	0.00	46.84
21319	21319	0.00	47.72
21434	22334	1.55	47.19
21830	21998	1.60	46.72
21998	21998	0.00	47.92
22264	22334	0.92	46.98
22331	22331	0.00	47.14
22332	22332	0.00	46.32
22333	22333	0.00	47.30
22334	22334	0.00	47.16
23022	22334	1.95	47.21
20968	20968	0.00	43.32
21314	21998	7.10	42.89
21442	21998	8.25	42.89
23725	20968	8.83	43.00
22266	22266	0.00	39.40
22398	22398	0.00	39.48
22399	22399	0.00	39.60
22400	22400	0.00	39.45
22401	22401	0.00	39.43
22402	22402	0.00	39.48
22403	22403	0.00	39.94
21381	21054	6.03	29.94
20896	20896	0.00	40.74
21318	20896	20.99	40.55
21435	20896	16.83	40.56

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Chloral hydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20322-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chloral hydrate; Chlorali hydras

Special notes

When selecting the *Chloral hydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Chloral hydrate	5	6	114

Second-stage model

For differentiation of the substance/substance group *Chloral hydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chloral hydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Chloral hydrate	13213311	21309	40	20130712
Caelo	Chloral hydrate	15448318	22963	40	1704462
Caelo	Chloral hydrate	16355802	23094	40	20170112
Fagron	Chloral hydrate	13F06-N07	21231	40	20130626
Fagron	Chloral hydrate	17E05-B05-335580	23572	40	20170623

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Chloral hydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 489 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Chloral hydrate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Chloral hydrate	154483	23355	40
Caelo	Chloral hydrate	172506	23646	40
Caelo	Chloral hydrate	172477	23678	40
Caelo	Chloral hydrate	190914	24556	40
Caelo	Chloral hydrate	192361	24882	40
Caelo	Chloral hydrate	192872	24891	40
Caelo	Chloral hydrate	172477	23815	40

- 118 862 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 401 spectra from 175 *Apo-Ident* customers from 118 batches from the substance/substance group *Chloral hydrate*.
- Among them are spectra of independent samples from 114 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Chloral hydrate	17346301	1
Caelo	Chloral hydrate	14038311	4
Caelo	Chloral hydrate	17346306	26
Caelo	Chloral hydrate	17314322	2
Caelo	Chloral hydrate	12017512	1
Caelo	Chloral hydrate	12017503	1
Caelo	Chloral hydrate	14101307	1
Caelo	Chloral hydrate	13002425	2
Caelo	Chloral hydrate	25021401	1
Caelo	Chloral hydrate	14038306	1
Caelo	Chloral hydrate	1403815	1
Caelo	Chloral hydrate	14218704	3
Caelo	Chloral hydrate	14218701	1
Caelo	Chloral hydrate	3121403	1
Caelo	Chloral hydrate	17121402	1
Caelo	Chloral hydrate	14218710	1
Caelo	Chloral hydrate	14218714	4
Caelo	Chloral hydrate	14218712	1
Caelo	Chloral hydrate	14218720	1
Caelo	Chloral hydrate	15083701	2
Caelo	Chloral hydrate	15083703	8
Caelo	Chloral hydrate	15083704	1
Caelo	Chloral hydrate	15166503	4
Caelo	Chloral hydrate	15166506	7
Caelo	Chloral hydrate	15163901	1
Caelo	Chloral hydrate	15166507	10
Caelo	Chloral hydrate	2826	1
Caelo	Chloral hydrate	15166513	2
Caelo	Chloral hydrate	160906C	1
Caelo	Chloral hydrate	15448304	2
Caelo	Chloral hydrate	15448307	5

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Supplier	Substance	Batch	Spectra
Caelo	Chloral hydrate	16248703	1
Caelo	Chloral hydrate	15448313	8
Caelo	Chloral hydrate	15448315	5
Caelo	Chloral hydrate	15448314	6
Caelo	Chloral hydrate	6051703	1
Caelo	Chloral hydrate	16355803	1
Caelo	Chloral hydrate	16355804	2
Caelo	Chloral hydrate	15448325	2
Caelo	Chloral hydrate	17247702	13
Caelo	Chloral hydrate	16355811	1
Caelo	Chloral hydrate	17346302	13
Caelo	Chloral hydrate	30081807	1
Caelo	Chloral hydrate	17346307	8
Caelo	Chloral hydrate	17346311	2
Caelo	Chloral hydrate	17314318	1
Caelo	Chloral hydrate	19091401	1
Caelo	Chloral hydrate	19236103	1
Caelo	Chloral hydrate	19236102	2
Caelo	Chloral hydrate	19287206	1
Caelo	Chloral hydrate	17346310	6
Caelo	Chloral hydrate	19091405	1
Caelo	Chloral hydrate	15448322	5
Caelo	Chloral hydrate	15166502	3
Caelo	Chloral hydrate	14038301	2
Caelo	Chloral hydrate	15448310	1
Caelo	Chloral hydrate	17346301	17
Caelo	Chloral hydrate	173463021	1
Caelo	Chloral hydrate	14218709	5
Caelo	Chloral hydrate	17520601	1
Caelo	Chloral hydrate	192872003	1
Caelo	Chloral hydrate	17550601	1
Caelo	Chloral hydrate	18054001	1
Caelo	Chloral hydrate	3299	1
Caelo	Chloral hydrate	3333	1
Caelo	Chloral hydrate	13d22-n11	1
Caelo	Chloral hydrate	19287201	1
Caelo	Chloral hydrate	19091408	1
Caelo	Chloral hydrate	17314301	3
Caelo	Chloral hydrate	14218711	1
Caelo	Chloral hydrate	14218719	4
Caelo	Chloral hydrate	15083705	1
Caelo	Chloral hydrate	15448312	10
Caelo	Chloral hydrate	15448320	4
Caelo	Chloral hydrate	17247704	5
Caelo	Chloral hydrate	15448326	7
Caelo	Chloral hydrate	14218705	3
Caelo	Chloral hydrate	15448306	7
Caelo	Chloral hydrate	15448321	4
Caelo	Chloral hydrate	17346303	5
Caelo	Chloral hydrate	3449	1
Caelo	Chloral hydrate	14218713	1
Caelo	Chloral hydrate	15448324	9
Caelo	Chloral hydrate	17346309	7
Caelo	Chloral hydrate	19091404	2
Caelo	Chloral hydrate	15448303	3
Caelo	Chloral hydrate	15166508	5
Caelo	Chloral hydrate	17314312	1
Caelo	Chloral hydrate	19091409	1
Caesar	Chloral hydrate	15166501	1
Caesar & Loretz GmbH	Chloral hydrate	17346301	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Chloral hydrate	17314319	1
Caesar & Loretz GmbH	Chloral hydrate	17314317	1
Caesar/Phoenix	Chloral hydrate	17250601	1
Cealo/ Alliance	Chloral hydrate	17247702	1
Ebert KKH 10.10.16	Chloral hydrate	15448308	1
Euro OTC	Chloral hydrate	15448318	1
Euro OTC	Chloral hydrate	16122001	1
Fagron	Chloral hydrate	12H06_N08	1
Fagron	Chloral hydrate	12H06-N08	6
Fagron	Chloral hydrate	12C26-M04	1
Fagron	Chloral hydrate	11D13-N07	1
Fagron	Chloral hydrate	11J05-N01	1
Fagron	Chloral hydrate	12H06N08	2
Fagron	Chloral hydrate	13F06-N070631/786	1
Fagron	Chloral hydrate	12H06N8	1
Fagron	Chloral hydrate	13D22-N11	1
Fagron	Chloral hydrate	13K05-B13	1
Fagron	Chloral hydrate	14218710	1
Fagron	Chloral hydrate	14218712	1
Fagron	Chloral hydrate	160609/1	1
Fagron	Chloral hydrate	18F15-B01-355393	1
Fagron	Chloral hydrate	18F15-B01-355394	1
Fagron	Chloral hydrate	12H06-N080101/1612	1
Fagron	Chloral hydrate	15166505	1
Fagron	Chloral hydrate	17J31-B02-342155	1
Gehe	Chloral hydrate	15448326	1
Gehe	Chloral hydrate	17247704	2
Gehe	Chloral hydrate	17346301	1
GEHE	Chloral hydrate	15448312	1
Caelo	Chloral hydrate	15166501	2
Ichthyol	Chloral hydrate	15448314	1
Ichthyol GmbH	Chloral hydrate	13002425	2
Kehr	Chloral hydrate	17346302	1
L12	Chloral hydrate	17346301	1
Noweda	Chloral hydrate	19091404	1
Fagron	Chloral hydrate	12H06-N080160/161	1
Fagron	Chloral hydrate	17346301	1
Caelo	Chloral hydrate	15166505	6
Noweda29.04.2015	Chloral hydrate	15083701	2
Phoenix	Chloral hydrate	15448318	1
Phoenix	Chloral hydrate	3187	1
Caelo	Chloral hydrate	12017518	1
Phönix	Chloral hydrate	17346303	3
Phönix	Chloral hydrate	17346301	1
Phönix	Chloral hydrate	17346311	5
Phönix Gotha	Chloral hydrate	13F06-N07	2
Phönix Gotha	Chloral hydrate	14038302	1
Caelo	Chloral hydrate	17250601	9
Sanacorp	Chloral hydrate	12H06-N08	3
Sanacorp	Chloral hydrate	14218705	1
Sanacorp	Chloral hydrate	17346301	1
Sanacorp	Chloral hydrate	17346306	1
Fagron	Chloral hydrate	12C26-M05	1
Caelo	Chloral hydrate	15448318	9
Caelo	Chloral hydrate	13213311	1
Fagron	Chloral hydrate	13F06-N07	2

- 110846 spectra from 742 *Apo-Ident* customers from a total of 31 773 batches from a further 706

substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chloral hydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chloral hydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	280	0	118 862
Type C	0	394	7	110 846

The substance/substance group *Chloral hydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	98.2544 % (> 97.5062 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chloral hydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium tetraborate	45.74	—
Levothyroxin sodium	48.51	—
Hyaluronic acid sodium salt	54.70	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chloral hydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21231	22963	6.30	48.50
21309	22963	5.51	48.60
22963	22963	0.00	49.41
23094	22963	4.24	48.51
23572	22963	3.35	49.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Chloramphenicol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20097-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chloramphenicol; Chloramphenicolum

Special notes

When selecting the *Chloramphenicol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Chloramphenicol	10	7	238

Second-stage model

For differentiation of the substance/substance group *Chloramphenicol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chloramphenicol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Chloramphenicol	11370716	20787	40	20120202
Caelo	Chloramphenicol	12248507	20807	40	20120831
Caelo	Chloramphenicol	13080924	21701	60	1509287
Caelo	Chloramphenicol	14346908	21988	60	20150115
Euro OTC	Chloramphenicol	1209019-02	20813	80	20130408
Euro OTC	Chloramphenicol	1209019-02	20815	80	20130408
Euro OTC	Chloramphenicol	1407043-01	21752	60	20140903
Euro OTC	Chloramphenicol	1602002	22367	45	20160309*
Fagron	Chloramphenicol	11F20-N05	20777	120	1412249
Fagron	Chloramphenicol	13A11-N02	20822	40	20130125
Fagron	Chloramphenicol	14E01-B02-308559	21910	60	20140513

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 685 spectra of 11 reference samples from the substance/substance group *Chloramphenicol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 004 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 280 spectra of 7 reference samples from the substance/substance group *Chloramphenicol*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Chloramphenicol	15358906	22961	40
Caelo	Chloramphenicol	162786	23353	40
Caelo	Chloramphenicol	180178	24049	40
Caelo	Chloramphenicol	192260	24892	40
Euro OTC	Chloramphenicol	1704021	23392	40
Euro OTC	Chloramphenicol	1903028	24625	40
Fagron	Chloramphenicol	16I12-B07-327124	22962	40

- 118862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1390 spectra from 472 *Apo-Ident* customers from 252 batches from the substance/substance group *Chloramphenicol*.
- Among them are spectra of independent samples from 236 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Chloramphenicol	1704021-01	7
AHD	Chloramphenicol	12248507	1
AHD	Chloramphenicol	12248509	1
AHD	Chloramphenicol	13080904	1
AHD	Chloramphenicol	14346912	1
AHD	Chloramphenicol	18017807	1
AHDE 20.08.15	Chloramphenicol	DY00912128	1
Euro OTC	Chloramphenicol	DY00914151	1
Euro OTC	Chloramphenicol	15358906	1
Alliance 15.04.2015 Ek ...	Chloramphenicol	1407043-01	1
Alliance Health	Chloramphenicol	1209019-02	1
anzag	Chloramphenicol	15358907	1
Anzag	Chloramphenicol	1302024-01	1
Anzag	Chloramphenicol	1308017-02	1
Anzag	Chloramphenicol	14346924	2
Anzag	Chloramphenicol	1602002-03	1
ANZAG	Chloramphenicol	1308017-02	1
Anzag 03.04.13 ek: 3,18EUR	Chloramphenicol	12248501	1
Anzag ek:2.98EUR 25.08.12	Chloramphenicol	11370711	1
Bombastus	Chloramphenicol	1308017-01	1
Bombastus	Chloramphenicol	1602002-03	1
Bombastus	Chloramphenicol	1704021-01	1
Caelo	Chloramphenicol	13080303	1
Caelo	Chloramphenicol	1436918	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Chloramphenicol	10341717	1
Caelo	Chloramphenicol	12072606	1
Caelo	Chloramphenicol	11370703	2
Caelo	Chloramphenicol	10341703	1
Caelo	Chloramphenicol	11370711	10
Caelo	Chloramphenicol	1137070	1
Caelo	Chloramphenicol	12G02-N01	2
Caelo	Chloramphenicol	4712Q-01259	1
Caelo	Chloramphenicol	11370713	3
Caelo	Chloramphenicol	11370712	4
Caelo	Chloramphenicol	10341711	2
Caelo	Chloramphenicol	10341707	1
Caelo	Chloramphenicol	12g02n01	1
Caelo	Chloramphenicol	11370717	2
Caelo	Chloramphenicol	12248506	8
Caelo	Chloramphenicol	12248505	2
Caelo	Chloramphenicol	310311	1
Caelo	Chloramphenicol	1302024-01	1
Caelo	Chloramphenicol	1302024-02	2
Caelo	Chloramphenicol	13A31-B02	1
Caelo	Chloramphenicol	20102012J1	1
Caelo	Chloramphenicol	28011401	1
Caelo	Chloramphenicol	11031402	1
Caelo	Chloramphenicol	13080903	8
Caelo	Chloramphenicol	13080904	5
Caelo	Chloramphenicol	DY130525	2
Caelo	Chloramphenicol	140704301	2
Caelo	Chloramphenicol	13080923	11
Caelo	Chloramphenicol	13080917	4
Caelo	Chloramphenicol	13080918	2
Caelo	Chloramphenicol	13080921	2
Caelo	Chloramphenicol	14346901	2
Caelo	Chloramphenicol	14346904	4
Caelo	Chloramphenicol	14346907	8
Caelo	Chloramphenicol	14346903	1
Caelo	Chloramphenicol	8701	1
Caelo	Chloramphenicol	14346912	3
Caelo	Chloramphenicol	14346910	13
Caelo	Chloramphenicol	14346913	8
Caelo	Chloramphenicol	14346911	22
Caelo	Chloramphenicol	14356910	1
Caelo	Chloramphenicol	130416-1	1
Caelo	Chloramphenicol	130416-2	1
Caelo	Chloramphenicol	14246917	1
Caelo	Chloramphenicol	3081602	1
Caelo	Chloramphenicol	1602002-01	4
Caelo	Chloramphenicol	14346914	4
Caelo	Chloramphenicol	150528C	1
Caelo	Chloramphenicol	15358903	3
Caelo	Chloramphenicol	1602002-02	2
Caelo	Chloramphenicol	15358906	11
Caelo	Chloramphenicol	160200201	1
Caelo	Chloramphenicol	15358913	23
Caelo	Chloramphenicol	15358911	1
Caelo	Chloramphenicol	153589	1
Caelo	Chloramphenicol	16278602	4
Caelo	Chloramphenicol	16278608	9
Caelo	Chloramphenicol	16278609	21
Caelo	Chloramphenicol	17A23-B08-337138	1
Caelo	Chloramphenicol	16278610	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Chloramphenicol	1704021-02	2
Caelo	Chloramphenicol	17343803	16
Caelo	Chloramphenicol	1704021-03	1
Caelo	Chloramphenicol	18017804	4
Caelo	Chloramphenicol	18017811	7
Caelo	Chloramphenicol	8017811	1
Caelo	Chloramphenicol	19226003	5
Caelo	Chloramphenicol	150203603	1
Caelo	Chloramphenicol	17343802	8
Caelo	Chloramphenicol	1137714	1
Caelo	Chloramphenicol	1137004	1
Caelo	Chloramphenicol	12248520	7
Caelo	Chloramphenicol	1627898	1
Caelo	Chloramphenicol	82853399	1
Caelo	Chloramphenicol	16278611	2
Caelo	Chloramphenicol	15358905	20
Caelo	Chloramphenicol	11370706	3
Caelo	Chloramphenicol	1407043-01	1
Caelo	Chloramphenicol	16278609/180420CA	1
Caelo	Chloramphenicol	14E01-B02-296623	1
Caelo	Chloramphenicol	18025702	2
Caelo	Chloramphenicol	3125204	1
Caelo	Chloramphenicol	13080902	1
Caelo	Chloramphenicol	1308017-01	1
Caelo	Chloramphenicol	1704021-04	2
Caelo	Chloramphenicol	15358907	2
Caelo	Chloramphenicol	4412Q-01259	1
Caelo	Chloramphenicol	14346906	3
Caelo	Chloramphenicol	DY00911233	1
Caelo	Chloramphenicol	18017802	2
Caelo	Chloramphenicol	14346917	7
Caelo	Chloramphenicol	1062002-04	1
Caelo	Chloramphenicol	1903028-01	2
Caelo	Chloramphenicol	11370715	1
Caelo	Chloramphenicol	12248509	12
Caelo	Chloramphenicol	93323801	1
Caelo	Chloramphenicol	15358909	6
Caelo	Chloramphenicol	1602002-03	1
Caelo	Chloramphenicol	18017807	4
Caelo	Chloramphenicol	18017814	2
Caelo	Chloramphenicol	13080925	11
Caelo	Chloramphenicol	12248524	7
Caelo	Chloramphenicol	11370714	2
Caelo	Chloramphenicol	14346918	17
Caelo	Chloramphenicol	1502036-03	2
Caelo	Chloramphenicol	14346924	5
Caelo	Chloramphenicol	1535896	1
Caelo	Chloramphenicol	15358914	16
Caelo	Chloramphenicol	170402101	1
Caelo	Chloramphenicol	16278009	1
Caelo	Chloramphenicol	13080907	13
Caelo	Chloramphenicol	1436908	1
Caelo	Chloramphenicol	15358908	10
Caelo	Chloramphenicol	1903028-041	1
Caelo	Chloramphenicol	18017810	3
Caelo	Chloramphenicol	13080915	1
Caelo	Chloramphenicol	1502036-02	1
Caelo	Chloramphenicol	14346922	1
Caelo	Chloramphenicol	15358912	9
Caelo	Chloramphenicol	16358909	1

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Supplier	Substance	Batch	Spectra
Caelo	Chloramphenicol	16278601	1
Caelo	Chloramphenicol	16278606	6
Caelo	Chloramphenicol	16278612	15
Caelo	Chloramphenicol	1627862	1
Caelo	Chloramphenicol	18017806	14
Caelo	Chloramphenicol	18017809	18
Caelo	Chloramphenicol	1502036-01	3
Caelo	Chloramphenicol	130809	1
Caelo	Chloramphenicol	1434608	1
Caecolo / Anzag	Chloramphenicol	15358914	1
Caesar & Loretz GmbH	Chloramphenicol	11370711	1
Caesar & Loretz GmbH	Chloramphenicol	18017806	1
Caesar & Loretz GmbH	Chloramphenicol	18017809	1
Caesar & Loretz GmbH	Chloramphenicol	19226003	1
Caesar und Loretz GmbH	Chloramphenicol	19226002	1
Caolo- Noweda	Chloramphenicol	14346908	1
Cealo	Chloramphenicol	1602002-03	1
Eu Rho Pharm/K	Chloramphenicol	1704021-04	1
Eurho	Chloramphenicol	1704087-03	1
EuRho	Chloramphenicol	216A-01259	1
EuRho	Chloramphenicol	1704021-01	2
EuRho	Chloramphenicol	1704021-04	1
EuRho / 20	Chloramphenicol	1502036-01	1
Eurho Phönix	Chloramphenicol	1704021-02	1
EuRho/ Phönix	Chloramphenicol	1704021-01	2
EuRho/Noweda	Chloramphenicol	1704021-02	1
EuRho/Phönix	Chloramphenicol	123012-01	1
EuRho/Phönix	Chloramphenicol	1308017-01	1
EuRho/Phönix	Chloramphenicol	1903028-02	1
EuRho/Sanacorp	Chloramphenicol	1704021-01	1
Euro OCT	Chloramphenicol	1203012-02	1
Euro OTC	Chloramphenicol	1509211259	1
Euro OTC	Chloramphenicol	1203012-02	11
Euro OTC	Chloramphenicol	2121211203012-0	1
Euro OTC	Chloramphenicol	1302024-02	7
Euro OTC	Chloramphenicol	1308017-01	10
Euro OTC	Chloramphenicol	130801701	1
Euro OTC	Chloramphenicol	130801702	2
Euro OTC	Chloramphenicol	DY130525	1
Euro OTC	Chloramphenicol	120250	1
Euro OTC	Chloramphenicol	13111410	1
Euro OTC	Chloramphenicol	140704301	4
Euro OTC	Chloramphenicol	1602002-02	24
Euro OTC	Chloramphenicol	10061707	1
Euro OTC	Chloramphenicol	1602002-04	1
Euro OTC	Chloramphenicol	15358914	1
Euro OTC	Chloramphenicol	1704021-015505	1
Euro OTC	Chloramphenicol	1903028-01	22
Euro OTC	Chloramphenicol	1203012-12	1
Euro OTC	Chloramphenicol	1407043	1
Euro OTC	Chloramphenicol	170402101	1
Euro OTC	Chloramphenicol	1903028_01	1
Euro OTC	Chloramphenicol	1704021_02	1
Euro OTC	Chloramphenicol	1704021-02	33
Euro OTC	Chloramphenicol	170402103	1
Euro OTC	Chloramphenicol	120901902	3
Euro OTC	Chloramphenicol	150203603	1
Euro OTC	Chloramphenicol	14101717	1
Euro OTC	Chloramphenicol	1308017-02	9
Euro OTC	Chloramphenicol	1502036	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Chloramphenicol	1107002-01	2
Euro OTC	Chloramphenicol	110700202	1
Euro OTC	Chloramphenicol	1209019-01	5
Euro OTC	Chloramphenicol	T02-55/1407043-01	1
Euro OTC	Chloramphenicol	1704021-04	29
Euro OTC	Chloramphenicol	170402102	1
Euro OTC	Chloramphenicol	1704021-03	26
Euro OTC	Chloramphenicol	1107002-02	1
Euro OTC	Chloramphenicol	1203012-01	7
Euro OTC	Chloramphenicol	1704021	2
Euro OTC	Chloramphenicol	1701021-04	1
Euro OTC	Chloramphenicol	1704021-01	62
Euro OTC	Chloramphenicol	314Q1259	1
Euro OTC	Chloramphenicol	1602002-03	26
Caelo	Chloramphenicol	1203012-02	1
Euro OTC	Chloramphenicol	1502036-02	16
Euro OTC	Chloramphenicol	1502036022016030911	1
Euro OTC	Chloramphenicol	170421-01	1
Euro OTC	Chloramphenicol	1704021-01A	1
Euro OTC	Chloramphenicol	DY00912128	3
Euro OTC	Chloramphenicol	16020002-03	1
Euro OTC	Chloramphenicol	1602002-01	38
Euro OTG	Chloramphenicol	1502036-01	1
Euro/ Sanacorp	Chloramphenicol	1308017-02	1
EUro/AHD	Chloramphenicol	1209019-01	1
EUro/AHD	Chloramphenicol	1209019-02	1
Euro/Alliance Healthcare	Chloramphenicol	1502036-01	1
Euro/Noweda	Chloramphenicol	1602002-02	1
Euro/Phönix	Chloramphenicol	1502036-03	1
Euro OTC	Chloramphenicol	1012013-01	2
Euro OTC	Chloramphenicol	1209010-02	3
Euro OTC	Chloramphenicol	1502036-03	22
Euro OTC	Chloramphenicol	1602002-07	1
Euro OTC	Chloramphenicol	17044021-01	1
Euro OTC	Chloramphenicol	160200203	2
Euro OTC	Chloramphenicol	1302024-01	12
Euro OTC	Chloramphenicol	1903028-02	7
Euro OTC	Chloramphenicol	190302801	1
EurPS	Chloramphenicol	1502036-01	2
Fagron	Chloramphenicol	13A31-B02-286709	2
Fagron	Chloramphenicol	11J14-N03	1
Fagron	Chloramphenicol	12L11-N06	9
Fagron	Chloramphenicol	13A11N02	1
Fagron	Chloramphenicol	12F01-N23	1
Fagron	Chloramphenicol	DY00911233	4
Fagron	Chloramphenicol	13A31-B02-286708	4
Fagron	Chloramphenicol	13A31-B02-290300	3
Fagron	Chloramphenicol	14E01-B02-306146	7
Fagron	Chloramphenicol	14E01B02296624	2
Fagron	Chloramphenicol	14E01-B02-296625	1
Fagron	Chloramphenicol	16/12-B07	1
Fagron	Chloramphenicol	16112-B07-326036	1
Fagron	Chloramphenicol	1602002-02	1
Fagron	Chloramphenicol	16/12-B07-332100	1
Fagron	Chloramphenicol	16I12-B07-326037	1
Fagron	Chloramphenicol	1202500003	1
Fagron	Chloramphenicol	1602002-01	2
Fagron	Chloramphenicol	17A23-B-08-336728	1
Fagron	Chloramphenicol	14E01-B02-296624	5
Fagron	Chloramphenicol	13A31-B02_286708	1

continued on the next page

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Supplier	Substance	Batch	Spectra
Fagron	Chloramphenicol	13A31-B02-290263	1
Fagron	Chloramphenicol	1602002-03	1
Fagron	Chloramphenicol	17A23B08337138	1
Fagron	Chloramphenicol	17A23-B08	1
Fagron	Chloramphenicol	17A23-B08-336728	2
Fagron	Chloramphenicol	14e01-b02-296624	1
Fagron	Chloramphenicol	12B13-N06	6
Fagron	Chloramphenicol	2111I-01259	1
Fagron	Chloramphenicol	14E01-B02	5
Fagron	Chloramphenicol	15G14-B04-322516	4
Fagron	Chloramphenicol	11/14-N03	2
Fagron	Chloramphenicol	12G02-N01	9
Fagron	Chloramphenicol	16112-b07-327124	1
Fagron	Chloramphenicol	14E01-B02-296623	1
Fagron	Chloramphenicol	13A31-B02	8
Fiebig	Chloramphenicol	1502036-01	1
Fiebig	Chloramphenicol	1602002-01	1
Fiebig	Chloramphenicol	15358913	1
Fiebig	Chloramphenicol	16278608	1
Fiebig	Chloramphenicol	16278609	1
Fiebig	Chloramphenicol	16278612	1
Fiebig	Chloramphenicol	1734803	1
Fiebig	Chloramphenicol	18017810	1
Fiebig	Chloramphenicol	18017809	1
Finteler Apotheke	Chloramphenicol	15358913	1
Fischer/ Noweda	Chloramphenicol	1502036-03	1
Fragon	Chloramphenicol	12G02-N01	1
Gatt-Koller / Phoenix	Chloramphenicol	5615/12115211	1
Gehe	Chloramphenicol	1107002-02	1
Gehe	Chloramphenicol	1203012-01	1
Gehe	Chloramphenicol	1209019-02	1
Gehe	Chloramphenicol	1308017-02	1
Gehe	Chloramphenicol	15358906	1
Gehe	Chloramphenicol	15358909	1
Gehe	Chloramphenicol	1704021-02	1
Gehe	Chloramphenicol	18017811	1
Gehe	Chloramphenicol	1903028-01	1
GEHE	Chloramphenicol	160200202	1
GEHE	Chloramphenicol	16278608	1
GEHE	Chloramphenicol	15358914	1
GEHE	Chloramphenicol	17343803	1
GEHE	Chloramphenicol	18017806	1
GEHE	Chloramphenicol	18017811	1
GEHE	Chloramphenicol	19226002	1
Caelo	Chloramphenicol	12248525	7
Gehe - Hedinger	Chloramphenicol	1704021-01	1
Gehe 27.06.15/euro	Chloramphenicol	1502036-01	2
Caelo	Chloramphenicol	12248501	12
Caelo	Chloramphenicol	2181116	1
Euro OTC	Chloramphenicol	150203602	1
Gutenberg-Apotheke	Chloramphenicol	13A31-B02-286710	1
Kehr	Chloramphenicol	1704021-01	1
Caelo	Chloramphenicol	181017809	1
Mehta API	Chloramphenicol	181113082	1
Nanjing Baijingyu Pharm...	Chloramphenicol	14346917	1
Nanjing Baijingyu Pharm...	Chloramphenicol	13080908	2
Northeast Gen	Chloramphenicol	DY122127	1
Northeast General	Chloramphenicol	1407043-01	1
Northeast General	Chloramphenicol	1602002-02	1
Northeast General	Chloramphenicol	DY00914151	2

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Supplier	Substance	Batch	Spectra
Northeast General	Chloramphenicol	1704021-01	2
Northeast General / Gehe	Chloramphenicol	1602002-02	1
Northeast General/Noweda	Chloramphenicol	1502036-02	1
noweda	Chloramphenicol	13080908	1
Noweda	Chloramphenicol	11370712	1
Noweda	Chloramphenicol	1137014	1
Noweda	Chloramphenicol	12248509	1
Noweda	Chloramphenicol	14346901	2
Noweda	Chloramphenicol	14346910	1
Noweda	Chloramphenicol	1602002-02	1
Noweda	Chloramphenicol	1704021-01	2
Noweda	Chloramphenicol	16278609	1
Noweda	Chloramphenicol	1903028	1
Noweda	Chloramphenicol	19226002	1
Caelo	Chloramphenicol	13A31-B02-286709	1
Caelo	Chloramphenicol	14E01B02296624	1
Caelo	Chloramphenicol	16/12-Bo7-329313	1
Euro OTC	Chloramphenicol	150203601	5
Ph/Euro	Chloramphenicol	1704021-02	1
Phoe	Chloramphenicol	15358905	1
phoenix	Chloramphenicol	1903028	1
Phoenix	Chloramphenicol	13080903	1
Phoenix	Chloramphenicol	3087	1
Phoenix	Chloramphenicol	16278609	1
Phoenix	Chloramphenicol	1704021-01	1
Phoenix	Chloramphenicol	1704021-02	1
Phoenix	Chloramphenicol	18017814	1
PHOENIX 25.04.2014	Chloramphenicol	1308017-02	2
phoenix-06.11.18	Chloramphenicol	17343803	1
phönix	Chloramphenicol	15358912	1
Phönix	Chloramphenicol	10341716	1
Phönix	Chloramphenicol	13A11-N02	3
Phönix	Chloramphenicol	10341710	1
Phönix	Chloramphenicol	13A1-802	3
Phönix	Chloramphenicol	13080921	1
Phönix	Chloramphenicol	16i12-b07-327124	1
Phönix	Chloramphenicol	3157	1
Phönix	Chloramphenicol	1903028-02	1
PHÖNIX	Chloramphenicol	16278608	1
Phönix 11.11.2019	Chloramphenicol	19226003	1
Phönix 12.10.2019	Chloramphenicol	1903028-01	1
Phönix Gotha	Chloramphenicol	13080907	1
Caelo	Chloramphenicol	16258612	1
Fagron	Chloramphenicol	DY00912129	1
Caelo	Chloramphenicol	13080908	3
Sanacorp	Chloramphenicol	11370711	1
Sanacorp	Chloramphenicol	41/AKD23	1
Sanacorp	Chloramphenicol	120901902	1
Sanacorp	Chloramphenicol	12248501	1
Sanacorp	Chloramphenicol	41/AKD24	1
Sanacorp	Chloramphenicol	140704301	1
Sanacorp	Chloramphenicol	1502036-01	1
Sanacorp	Chloramphenicol	15358913	1
Sanacorp	Chloramphenicol	16278612	1
Sanacorp	Chloramphenicol	17343803	1
Sanacorp	Chloramphenicol	18017806	2
Sanacorp	Chloramphenicol	18017814	2
Caelo	Chloramphenicol	11370705	3
Euro OTC	Chloramphenicol	1502036-01	28
Caelo	Chloramphenicol	11370702	3

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Supplier	Substance	Batch	Spectra
Sanacorp/EuRho	Chloramphenicol	1704021-02	1
Fagron	Chloramphenicol	1502036-01	1
Spangro 12.05.2014	Chloramphenicol	1308017-01	1
Spangro 14.03.2014	Chloramphenicol	12248524	1
Spangro_22.11.2018	Chloramphenicol	17343803	1
Fagron	Chloramphenicol	12A11-N02	1
vdl	Chloramphenicol	12248501	1
VDL	Chloramphenicol	1308017-01	1
VDL	Chloramphenicol	140743-01	1
Caelo	Chloramphenicol	11370707	2
Caelo	Chloramphenicol	12248507	9
Caelo	Chloramphenicol	14346908	8
Caelo	Chloramphenicol	11370716	4
Caelo	Chloramphenicol	13080924	15
Euro OTC	Chloramphenicol	1209019-02	11
Euro OTC	Chloramphenicol		4
Euro OTC	Chloramphenicol	1407043-01	19
Fagron	Chloramphenicol	13A11-N02	6
Fagron	Chloramphenicol	14E01-B02-308559	7
Fagron	Chloramphenicol		2
Caelo	Chloramphenicol		1

- 109 857 spectra from 742 *Apo-Ident* customers from a total of 31 642 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chloramphenicol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chloramphenicol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	685	0	110 004
Type B	0	280	0	118 862
Type C	0	1379	11	109 857

The substance/substance group *Chloramphenicol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.1241 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	99.2086 % (> 98.9928 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chloramphenicol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	21.30	—
Oxytetracycline hydrochloride	31.67	—
Levothyroxin sodium	34.45	—
Eosin Y	49.14	—
Melatonin	56.56	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chloramphenicol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20787	20777	4.73	46.12
20807	20777	2.59	44.06
21988	21701	3.34	45.44
20777	20777	0.00	43.82
20813	20777	1.55	42.24
20815	20777	1.62	41.50
20822	20777	1.67	42.00
21701	21701	0.00	40.85
21752	22367	8.52	39.95
21910	22367	2.34	43.83
22367	22367	0.00	46.09

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Chlorhexidine diacetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20989-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chlorhexidine diacetate; Chlorhexidini acetat

Special notes

When selecting the *Chlorhexidine diacetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Chlorhexidine diacetate	8	2	96

Second-stage model

For differentiation of the substance/substance group *Chlorhexidine diacetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chlorhexidine diacetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Chlorhexidine di...	12142726	20989	40	1402685
Caelo	Chlorhexidine di...	12142727	21041	40	20120711
Caelo	Chlorhexidine di...	154389	22456	60	20160309*
Caelo	Chlorhexidine di...	15438914	22900	40	1704392
Caelo	Chlorhexidine di...	15438914	22951	40	20160309
Caelo	Chlorhexidine di...	15438913	23041	40	20160309*
Caelo	Chlorhexidine di...	154389	23042	40	20160309*
Caelo	Chlorhexidine di...	154389	23043	40	20160309*
Caelo	Chlorhexidine di...	15438909	23044	40	20160309*
Caelo	Chlorhexidine di...	154389	23048	40	20160309*
Fagron	Chlorhexidine di...	14I08-B02-306223	22280	60	20140922
Fagron	Chlorhexidine di...	14I08-B02-306223	22280SI	40	20140922
Fagron	Chlorhexidine di...	15J02-B08-322916	22946	40	20151104
Fagron	Chlorhexidine di...	15J02-B08-322916	22947	40	20151104

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 600 spectra of 14 reference samples from the substance/substance group *Chlorhexidine diacetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 089 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Chlorhexidine diacetate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Chlorhexidine diacetate	152610	23045	40
Caelo	Chlorhexidine diacetate	171858	23640	40
Caelo	Chlorhexidine diacetate	15438914	22951SI [†]	40
Fagron	Chlorhexidine diacetate	15J02-B08-322916	22947SI [†]	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 538 spectra from 306 *Apo-Ident* customers from 102 batches from the substance/substance group *Chlorhexidine diacetate*.
- Among them are spectra of independent samples from 95 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Chlorhexidine diacetate	17185812	1
AHL	Chlorhexidine diacetate	15438903	1
Alliance Healthcare	Chlorhexidine diacetate	12177510	1
Anzag	Chlorhexidine diacetate	70558377	1
Anzag	Chlorhexidine diacetate	12177505	1
Bomastus / Alliance Hea...	Chlorhexidine diacetate	17185804	1
Caelo	Chlorhexidine diacetate	11204401	3
Caelo	Chlorhexidine diacetate	123456	1
Caelo	Chlorhexidine diacetate	15261005	6
Caelo	Chlorhexidine diacetate	17185802	3
Caelo	Chlorhexidine diacetate	11204405	1
Caelo	Chlorhexidine diacetate	11204406	2
Caelo	Chlorhexidine diacetate	10154421	1
Caelo	Chlorhexidine diacetate	91139389	1
Caelo	Chlorhexidine diacetate	9113904	2
Caelo	Chlorhexidine diacetate	10154407	1
Caelo	Chlorhexidine diacetate	12177505	3
Caelo	Chlorhexidine diacetate	9113903	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Chlorhexidine diacetate	12177510	8
Caelo	Chlorhexidine diacetate	10154424	1
Caelo	Chlorhexidine diacetate	12142702	2
Caelo	Chlorhexidine diacetate	12142705	3
Caelo	Chlorhexidine diacetate	12142704	6
Caelo	Chlorhexidine diacetate	12142725	6
Caelo	Chlorhexidine diacetate	12177504	1
Caelo	Chlorhexidine diacetate	31032014B	1
Caelo	Chlorhexidine diacetate	13177001	5
Caelo	Chlorhexidine diacetate	12142734	13
Caelo	Chlorhexidine diacetate	13177002	10
Caelo	Chlorhexidine diacetate	23012015D	1
Caelo	Chlorhexidine diacetate	13177008	4
Caelo	Chlorhexidine diacetate	1072015C	1
Caelo	Chlorhexidine diacetate	15261012	8
Caelo	Chlorhexidine diacetate	15261011	1
Caelo	Chlorhexidine diacetate	12177503	2
Caelo	Chlorhexidine diacetate	160912CH	1
Caelo	Chlorhexidine diacetate	10154430	2
Caelo	Chlorhexidine diacetate	15438902	8
Caelo	Chlorhexidine diacetate	1543909	1
Caelo	Chlorhexidine diacetate	17185803	5
Caelo	Chlorhexidine diacetate	17185807	15
Caelo	Chlorhexidine diacetate	17185804	21
Caelo	Chlorhexidine diacetate	17185811	17
Caelo	Chlorhexidine diacetate	17188504	1
Caelo	Chlorhexidine diacetate	17325803	18
Caelo	Chlorhexidine diacetate	2195172	1
Caelo	Chlorhexidine diacetate	1735809	1
Caelo	Chlorhexidine diacetate	19121804	1
Caelo	Chlorhexidine diacetate	2195195	1
Caelo	Chlorhexidine diacetate	18072404	6
Caelo	Chlorhexidine diacetate	18072403	1
Caelo	Chlorhexidine diacetate	19097501	1
Caelo	Chlorhexidine diacetate	10154429	1
Caelo	Chlorhexidine diacetate	13177024	6
Caelo	Chlorhexidine diacetate	17185805	4
Caelo	Chlorhexidine diacetate	12177502	1
Caelo	Chlorhexidine diacetate	13177021	15
Caelo	Chlorhexidine diacetate	15261007	16
Caelo	Chlorhexidine diacetate	12142720	10
Caelo	Chlorhexidine diacetate	17185808	13
Caelo	Chlorhexidine diacetate	19097502	2
Caelo	Chlorhexidine diacetate	10154417	1
Caelo	Chlorhexidine diacetate	17185810	16
Caelo	Chlorhexidine diacetate	15261009	13
Caelo	Chlorhexidine diacetate	17326809	1
Caelo	Chlorhexidine diacetate	15438903	10
Caelo	Chlorhexidine diacetate	11204408	2
Caelo	Chlorhexidine diacetate	13177022	1
Caelo	Chlorhexidine diacetate	15261014	22
Caelo	Chlorhexidine diacetate	17185812	13
Caelo	Chlorhexidine diacetate	13177007	19
Caelo	Chlorhexidine diacetate	15438917	10
Caelo	Chlorhexidine diacetate	180130CA/17185804	1
Caelo	Chlorhexidine diacetate	15261004	2
Caelo	Chlorhexidine diacetate	1242720	1
Caelo	Chlorhexidine diacetate	13177009	1
Caelo	Chlorhexidine diacetate	17325801	3
Caelo	Chlorhexidine diacetate	17325808	5

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Supplier	Substance	Batch	Spectra
Caelo	Chlorhexidine diacetate	11204407	1
Caelo	Chlorhexidine diacetate	15438911	14
Caelo	Chlorhexidine diacetate	12142709	1
Caelo	Chlorhexidine diacetate	1317021	1
Caelo	Chlorhexidine diacetate	17325809	15
caesar	Chlorhexidine diacetate	15261014	1
Caesar & Loretz GmbH	Chlorhexidine diacetate	17325808	1
Caesar & Loretz GmbH	Chlorhexidine diacetate	18072404	2
Caesar & Loretz GmbH	Chlorhexidine diacetate	19097501	1
Caesar & Loretz GmbH / ...	Chlorhexidine diacetate	18072404	1
Caesar & Loretz GmbH / ...	Chlorhexidine diacetate	15261012	1
Caesar & Loretz GmbH, 4...	Chlorhexidine diacetate	12142720	1
Caesar & Loretz GmbH, A...	Chlorhexidine diacetate	17185812	1
Caesar&lorenz,Anzag	Chlorhexidine diacetate	12142704	1
cealo	Chlorhexidine diacetate	17185804	1
Cealo	Chlorhexidine diacetate	13177002	2
Ceasar & Loretz GmbH	Chlorhexidine diacetate	80104278	1
Cordes/Noweda	Chlorhexidine diacetate	15438914	1
Euro OTC	Chlorhexidine diacetate	17185810	3
Euro OTC	Chlorhexidine diacetate	15261004	1
Euro OTC	Chlorhexidine diacetate	10154430	1
Euro OTC	Chlorhexidine diacetate	1785805	1
Fagron	Chlorhexidine diacetate	12E14-N11	1
Fagron	Chlorhexidine diacetate	A-130037	1
Fagron	Chlorhexidine diacetate	13E03-B06-287926	2
Fagron	Chlorhexidine diacetate	13177008	1
Fagron	Chlorhexidine diacetate	13E03-B06	1
Fagron	Chlorhexidine diacetate	15J02-B08	1
Fagron	Chlorhexidine diacetate	17325801	1
Fagron	Chlorhexidine diacetate	1-8991-1-01-01	1
Fagron	Chlorhexidine diacetate	17185811	1
Fiebig	Chlorhexidine diacetate	15261014	1
Fiebig	Chlorhexidine diacetate	17185807	1
Gehe	Chlorhexidine diacetate	15438909	1
GEHE	Chlorhexidine diacetate	12142734	1
Fagron	Chlorhexidine diacetate	15261009	1
Jenne	Chlorhexidine diacetate	17185808	1
Jenne	Chlorhexidine diacetate	17185810	1
keine Angabe	Chlorhexidine diacetate	11204402	2
Medichem S.A. ES/Noweda	Chlorhexidine diacetate	13177007	1
Noweda	Chlorhexidine diacetate	12142720	1
Noweda	Chlorhexidine diacetate	12142727	1
Noweda	Chlorhexidine diacetate	15438911	2
Noweda	Chlorhexidine diacetate	17185805	1
Noweda	Chlorhexidine diacetate	17185808	1
Noweda	Chlorhexidine diacetate	1785803	1
Noweda	Chlorhexidine diacetate	17185811	1
Noweda	Chlorhexidine diacetate	17325808	1
Caelo	Chlorhexidine diacetate	12142715	3
Phoenix	Chlorhexidine diacetate	11204408	1
Phoenix	Chlorhexidine diacetate	12142726	1
Phoenix	Chlorhexidine diacetate	12142734	1
Phoenix	Chlorhexidine diacetate	13177002	1
Phoenix	Chlorhexidine diacetate	15438917	1
phönix	Chlorhexidine diacetate	15438911	1
Phönix	Chlorhexidine diacetate	Retest09113916	1
Phönix	Chlorhexidine diacetate	9113916	2
Phönix	Chlorhexidine diacetate	15438917	1
Phönix	Chlorhexidine diacetate	17325803	1
Caelo	Chlorhexidine diacetate	15261003	7

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Supplier	Substance	Batch	Spectra
Euro OTC	Chlorhexidine diacetate	17325809	1
Fagron	Chlorhexidine diacetate	15438901	1
Sanacorp	Chlorhexidine diacetate	12142734	1
Sanacorp	Chlorhexidine diacetate	7/AKD6	1
Sanacorp	Chlorhexidine diacetate	17185804	1
Sanacorp	Chlorhexidine diacetate	18072403	1
SANACORP	Chlorhexidine diacetate	19097502	1
Caelo	Chlorhexidine diacetate	12142704ok	1
Wepa/Wepa	Chlorhexidine diacetate	15438902	1
Caelo	Chlorhexidine diacetate	12142727	10
Caelo	Chlorhexidine diacetate	12142726	9
Caelo	Chlorhexidine diacetate	15438909	3
Caelo	Chlorhexidine diacetate	15438914	6
Fagron	Chlorhexidine diacetate	15J02-B08-322916	2
phönix	Chlorhexidine diacetate		1
Sanacorp	Chlorhexidine diacetate		1

- 110 709 spectra from 742 *Apo-Ident* customers from a total of 31 791 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chlorhexidine diacetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chlorhexidine diacetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	600	0	110 089
Type B	0	160	0	118 982
Type C	0	518	20	110 709

The substance/substance group *Chlorhexidine diacetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	96.2825 % (> 95.7249 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chlorhexidine diacetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	16.86	—
Levothyroxin sodium	31.81	—
Melatonin	37.04	—
Oxytetracycline hydrochloride	42.77	—
Chloramphenicol	50.52	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chlorhexidine diacetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23042	23042	0.00	37.71
23043	23043	0.00	37.90
23048	23048	0.00	37.78
22456	22456	0.00	37.63
20989	20989	0.00	37.29
21041	20989	4.84	37.13
22280	20989	3.09	37.93
22946	23044	3.05	37.73
22947	22456	2.88	37.58
23041	23041	0.00	37.73
23044	23044	0.00	37.67
22900	22900	0.00	38.74
22951	22900	3.00	38.51

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Chlorocresol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20185-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Chlorocresol; Chlorocresolum

Special notes

When selecting the *Chlorocresol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Chlorocresol	4	3	12

Second-stage model

For differentiation of the substance/substance group *Chlorocresol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chlorocresol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Chlorocresol	13275106	21512	60	20130828
Caelo	Chlorocresol	13275106	21513	60	20130828
Caelo	Chlorocresol	163378	23357	40	20170124*
Caelo	Chlorocresol	182523	24406	40	20180919*
Caelo	Chlorocresol	190837	24717	40	20190508*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Chlorocresol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Chlorocresol*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Chlorocresol	1211107	21306	40
Caelo	Chlorocresol	15114107	23411	40
Caelo	Chlorocresol	181360	24050	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 19 spectra from 14 *Apo-Ident* customers from 12 batches from the substance/substance group *Chlorocresol*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Chlorocresol	7061304	1
Caelo	Chlorocresol	12111017	2
Caelo	Chlorocresol	12111013	2
Caelo	Chlorocresol	2041513	1
Caelo	Chlorocresol	4613M-01260	1
Caelo	Chlorocresol	23415422	1
Caelo	Chlorocresol	20101808	1
Caelo	Chlorocresol	18027110	1
Caelo	Chlorocresol	10145239	3
Caelo	Chlorocresol	18027101	2
Caelo	Chlorocresol	15114107	1
Caesar & Loretz GmbH	Chlorocresol	12111017	1
Noweda	Chlorocresol	12111017	1
Caelo	Chlorocresol	13275117	1

- 111 228 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chlorocresol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chlorocresol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	116	4	119 022
Type C	0	18	1	111 228

The substance/substance group *Chlorocresol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	96.6667 % (> 94.1667 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chlorocresol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Propyl-4-hydroxybenzoate	21.50	—
Serine	26.14	—
Sodium cromoglicate	29.21	—
Levothyroxin sodium	38.43	—
Choline hydrogen tartrate	41.81	—
Guaifenesin	54.83	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chlorocresol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21513	24406	9.35	37.04
23357	23357	0.00	27.03
24717	24717	0.00	26.35
21512	24406	5.94	35.04
24406	24406	0.00	29.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Chlortetracycline hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20845-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Chlortetracycline hydrochloride; Chlortetracyclini hydrochloridum

Special notes

When selecting the *Chlortetracycline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Chlortetracycline hydrochloride	5	3	55

Second-stage model

For differentiation of the substance/substance group *Chlortetracycline hydrochloride* the following second-stage model is used:

- [Submodel 9](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Chlortetracycline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Chlortetracyclin...	1108051-02	21241	40	20111013
Euro OTC	Chlortetracyclin...	1604015	22541	40	20160510*
Euro OTC	Chlortetracyclin...	1910002	24959	40	20191107*
Fagron	Chlortetracyclin...	12K30-N07	20845	40	1405318
Fagron	Chlortetracyclin...	12K30-N07	21222	40	20121210
Fagron	Chlortetracyclin...	14J08-B07-307742	21877	60	20141029

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Chlortetracycline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 110 spectra of 3 reference samples from the substance/substance group *Chlortetracycline hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Chlortetracycline hydrochlor...	1604015-01	22975	40
Euro OTC	Chlortetracycline hydrochlor...	1803037	24092	40
Fagron	Chlortetracycline hydrochlor...	16B10-B09-329778	23571	30

- 119 032 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 233 spectra from 138 *Apo-Ident* customers from 64 batches from the substance/substance group *Chlortetracycline hydrochloride*.
- Among them are spectra of independent samples from 55 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ALH	Chlortetracycline hydrochlor...	16B10-B09-320304	1
Alliance Healthcare	Chlortetracycline hydrochlor...	12K30-N07	1
Anzag	Chlortetracycline hydrochlor...	1604015-01	1
Anzag: 07.09.12 ek:4.01	Chlortetracycline hydrochlor...	12C16-N01	1
Caelo	Chlortetracycline hydrochlor...	142008-03	1
Caelo	Chlortetracycline hydrochlor...	FC15100204	1
Caelo	Chlortetracycline hydrochlor...	16B10-B09-318088	1
Caelo	Chlortetracycline hydrochlor...	14J08-B07-303352	1
Caelo	Chlortetracycline hydrochlor...	16B10-B09-347439	1
Caelo	Chlortetracycline hydrochlor...	1108051-01	2
Caelo	Chlortetracycline hydrochlor...	1412008-01	1
Caelo	Chlortetracycline hydrochlor...	16B10-B09-322716	1
Caelo	Chlortetracycline hydrochlor...	141200802	1
Caelo	Chlortetracycline hydrochlor...	1803037-01	1
Caelo	Chlortetracycline hydrochlor...	14J08-B07-300249	1
Caelo	Chlortetracycline hydrochlor...	FC13030134	1
Caelo	Chlortetracycline hydrochlor...	1412008-02	1
Caelo	Chlortetracycline hydrochlor...	141200803	1
Caesar & Loretz GmbH	Chlortetracycline hydrochlor...	12C16-N01	1
EuRho	Chlortetracycline hydrochlor...	1803037-01	1
Euro	Chlortetracycline hydrochlor...	1108051-02	1
Euro OTC	Chlortetracycline hydrochlor...	110805102	1
Euro OTC	Chlortetracycline hydrochlor...	141200802	2
Euro OTC	Chlortetracycline hydrochlor...	16b10-b09-326865	1
Euro OTC	Chlortetracycline hydrochlor...	10I29-N04	1
Euro OTC	Chlortetracycline hydrochlor...	1412008/03	1
Euro OTC	Chlortetracycline hydrochlor...	1910002-01	2
Euro OTC	Chlortetracycline hydrochlor...	1803037_01	4
Euro OTC	Chlortetracycline hydrochlor...	1803037-01	7
Euro OTC	Chlortetracycline hydrochlor...	1412008-01	9

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Supplier	Substance	Batch	Spectra
Euro OTC	Chlortetracycline hydrochlor...	1412008-02	15
Euro OTC	Chlortetracycline hydrochlor...	1803037-03	2
Euro OTC	Chlortetracycline hydrochlor...	1604015-01	28
Euro OTC	Chlortetracycline hydrochlor...	2901009V-03	1
Euro OTC	Chlortetracycline hydrochlor...	1803037	1
Euro OTC	Chlortetracycline hydrochlor...	1108051-01	6
Euro OTC	Chlortetracycline hydrochlor...	700156	1
Euro OTC	Chlortetracycline hydrochlor...	4612Q-01155	1
Euro OTC	Chlortetracycline hydrochlor...	160401502	1
EURO Pharma	Chlortetracycline hydrochlor...	1108051-01	1
EUro/AHD	Chlortetracycline hydrochlor...	1108051-02	1
EuRo/Phönix	Chlortetracycline hydrochlor...	160401501	1
Euro OTC	Chlortetracycline hydrochlor...	1412008-03	5
Fagron	Chlortetracycline hydrochlor...	12k30-N07	1
Fagron	Chlortetracycline hydrochlor...	12C16-N01	1
Fagron	Chlortetracycline hydrochlor...	27121306	1
Fagron	Chlortetracycline hydrochlor...	FC13030134	1
Fagron	Chlortetracycline hydrochlor...	13/11-N07	4
Fagron	Chlortetracycline hydrochlor...	13111-N07	1
Fagron	Chlortetracycline hydrochlor...	FC11051038	1
Fagron	Chlortetracycline hydrochlor...	14J08-B07	4
Fagron	Chlortetracycline hydrochlor...	14J08-B07-303350	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-318088	5
Fagron	Chlortetracycline hydrochlor...	16B10-B09-322715	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-326865	1
Fagron	Chlortetracycline hydrochlor...	16b10-b09-336332	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-342410	2
Fagron	Chlortetracycline hydrochlor...	16B10-B09-348359	1
Fagron	Chlortetracycline hydrochlor...	13K26-N06	1
Fagron	Chlortetracycline hydrochlor...	FC15100204	4
Fagron	Chlortetracycline hydrochlor...	16B10-B09-322716	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-352970	3
Fagron	Chlortetracycline hydrochlor...	12H28N09	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-336332	5
Fagron	Chlortetracycline hydrochlor...	12H28-N09	4
Fagron	Chlortetracycline hydrochlor...	14J08-B07-303352	4
Fagron	Chlortetracycline hydrochlor...	14J08-B07-307100	6
Fagron	Chlortetracycline hydrochlor...	16B10-B09-320304	1
Fagron	Chlortetracycline hydrochlor...	16b10-b09	1
Fagron	Chlortetracycline hydrochlor...	14J08-B07-300250	8
Fagron	Chlortetracycline hydrochlor...	16B10-B09	5
Fagron	Chlortetracycline hydrochlor...	16B10-B09-331443	1
Fagron	Chlortetracycline hydrochlor...	16B10-B09-351565	1
Fiebig	Chlortetracycline hydrochlor...	1412008-01	1
Fiebig	Chlortetracycline hydrochlor...	1604015-01	1
Fagron	Chlortetracycline hydrochlor...	14J08B07307100	3
Gehe	Chlortetracycline hydrochlor...	16B10-B09	2
Gehe	Chlortetracycline hydrochlor...	16B10-B09-322716	1
Gehe	Chlortetracycline hydrochlor...	16B10-B09-322715	1
GEHE	Chlortetracycline hydrochlor...	1604015-01	1
Krieger	Chlortetracycline hydrochlor...	12C16-No1	1
Nachprüfung	Chlortetracycline hydrochlor...	1108051-01	1
Nachprüfung 2574	Chlortetracycline hydrochlor...	1108051-01	1
Noweda	Chlortetracycline hydrochlor...	12c16-n01	1
Caelo	Chlortetracycline hydrochlor...	1604015-01	3
Euro OTC	Chlortetracycline hydrochlor...	5113I01155	1
Phoenix	Chlortetracycline hydrochlor...	110805102	1
Phoenix	Chlortetracycline hydrochlor...	16B10-B09-322716	1
Phoenix	Chlortetracycline hydrochlor...	3407	1
Phönix	Chlortetracycline hydrochlor...	1108051-02	2

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Supplier	Substance	Batch	Spectra
Phönix	Chlortetracycline hydrochlor...	1803037-03	1
Euro OTC	Chlortetracycline hydrochlor...	141200803	1
Phönix/apo ident	Chlortetracycline hydrochlor...	1604015-01	1
Phönix/Euro	Chlortetracycline hydrochlor...	180303701	2
Sanacop	Chlortetracycline hydrochlor...	1412008-02	1
Sanacorp	Chlortetracycline hydrochlor...	1108051-01	1
Caelo	Chlortetracycline hydrochlor...		1
Euro OTC	Chlortetracycline hydrochlor...	1108051-02	7
Fagron	Chlortetracycline hydrochlor...	12K30-N07	9

- 111 014 spectra from 742 *Apo-Ident* customers from a total of 31 827 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Chlortetracycline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Chlortetracycline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	110	0	119 032
Type C	0	230	3	111 014

The substance/substance group *Chlortetracycline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 94.5455 %)
Type C	100.0000 % (> 99.8899 %)	98.7124 % (> 97.4249 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Chlortetracycline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	31.52	192.30
Oxytetracycline hydrochloride	31.84	—
Eosin Y	34.86	—
Tetracycline hydrochloride	35.29	—
Sulfogaiacol hydrate	53.66	—
⋮	⋮	⋮
Vancomycin hydrochloride	>50	384.93
Ethacridine lactate monohydrate	>50	574.66

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Chlortetracycline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22541	22541	0.00	34.82
24959	24959	0.00	42.72
20845	20845	0.00	38.37
21222	20845	2.86	39.06
21241	20845	5.44	37.26
21877	22541	6.35	36.96

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Cholesterol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20446-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cholesterol; Cholesterolum

Special notes

When selecting the *Cholesterol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cholesterol	5	3	70

Second-stage model

For differentiation of the substance/substance group *Cholesterol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cholesterol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Cholesterol	160444	22461	60	20160222*
Caelo	Cholesterol	16044415	23760	40	1804387
Fagron	Cholesterol	13F10-B40	21219	40	20131223
Fagron	Cholesterol	15J23-B03-325106	22971	40	20151103
Fagron	Cholesterol	17E17-B05-339074	23937	40	20170620

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Cholesterol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Cholesterol*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Cholesterol	13148703	21310	40
Caelo	Cholesterol	190549	24712	40
Fagron	Cholesterol	16G05-B03-331396	23522	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 130 spectra from 70 *Apo-Ident* customers from 75 batches from the substance/substance group *Cholesterol*.
- Among them are spectra of independent samples from 69 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Cholesterol	17K16-B11-352718	1
Caelo	Cholesterol	12155605	1
Caelo	Cholesterol	13056903	1
Caelo	Cholesterol	12248403	1
Caelo	Cholesterol	15301803	3
Caelo	Cholesterol	16G05-B03	1
Caelo	Cholesterol	27212	1
Caelo	Cholesterol	17K16-B11-345814	1
Caelo	Cholesterol	19054901	1
Caelo	Cholesterol	15G31-B05-312376	1
Caelo	Cholesterol	15J23-B03	1
Caelo	Cholesterol	15028303	1
Caelo	Cholesterol	13148704	1
Caelo	Cholesterol	14122501	2
Caelo	Cholesterol	14027201	1
Caelo	Cholesterol	14208602	1
Caelo	Cholesterol	11242103	1
Caelo	Cholesterol	15358801	5
Caelo	Cholesterol	15407101	2
Caelo	Cholesterol	15B09-B02-308259	1
Caelo	Cholesterol	19054903	1
Caelo	Cholesterol	15407102	2
Caelo	Cholesterol	16044408	2
Caesar & Loretz GmbH	Cholesterol	19194903	1
Fagron	Cholesterol	15G31-B05-312377	1
Ebert-Jacobi	Cholesterol	16044408	1
Ensbona /Alliance Healt...	Cholesterol	17E17-B05-339074	3
Fagro/EJ	Cholesterol	17K16-B11_348760	1
Fagron	Cholesterol	10B15-N07	1
Fagron	Cholesterol	10H24-N06	1
Fagron	Cholesterol	2013U-01270	1
Fagron	Cholesterol	13C25-N12	2
Fagron	Cholesterol	12I13-N02	2
Fagron	Cholesterol	14B27-B05	2
Fagron	Cholesterol	14G04-B02-300830	2

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Supplier	Substance	Batch	Spectra
Fagron	Cholesterol	14B27-B05-293550	1
Fagron	Cholesterol	14G04-B02-300831	1
Fagron	Cholesterol	14G04-B02	1
Fagron	Cholesterol	15G31-B05-312378	1
Fagron	Cholesterol	15G31-B05	2
Fagron	Cholesterol	15B09-B02-308259	3
Fagron	Cholesterol	15G31-B05-314182	2
Fagron	Cholesterol	15B09	1
Fagron	Cholesterol	15J23-B03-320483	4
Fagron	Cholesterol	15J23-B03	1
Fagron	Cholesterol	15J23-B03-322902	1
Fagron	Cholesterol	16G05-B03-333996	1
Fagron	Cholesterol	17E17-B05-337588	4
Fagron	Cholesterol	15G31-B05_316721	1
Fagron	Cholesterol	17E17-B05	1
Fagron	Cholesterol	16G05-B03-334366	1
Fagron	Cholesterol	17K16-B11-350557	3
Fagron	Cholesterol	17K16-B11-348761	1
Fagron	Cholesterol	27212	1
Fagron	Cholesterol	30969	1
Fagron	Cholesterol	15G31-B05-316721	2
Fagron	Cholesterol	17K16-B11-355385	5
Fagron	Cholesterol	18I03-B06-355386	1
Fagron	Cholesterol	19G12-B13-194214	1
Fagron	Cholesterol	17K16-B11-343922	2
Fagron	Cholesterol	13G10-N11	3
Fagron	Cholesterol	17K16-B11-348760	2
Fagron	Cholesterol	17K16-B11-352718	4
Fagron	Cholesterol	19g12-b13-194214	1
Fagron	Cholesterol	30197	1
Fagron	Cholesterol	12D02-N10	1
Fagron	Cholesterol	13F10-B40-289016	2
Fagron	Cholesterol	8J28-N10	1
Fagron	Cholesterol	11A17-N07	1
Fagron	Cholesterol	14B27-B05-293548	2
Fagron	Cholesterol	15B09-B02	1
Fagron	Cholesterol	15J23-B03-328249	2
Fagron	Cholesterol	15J23B03320483	1
Fagron	Cholesterol	19J18-B02-196477	1
Fagron/AllianceH.	Cholesterol	16G05-B03-328689	1
Noweda	Cholesterol	15J23-B03-320483	1
Fagron	Cholesterol	16G05-B03-331396	2
Caelo	Cholesterol	16044415	1
Fagron	Cholesterol	15J23-B03-325106	3
Fagron	Cholesterol	17E17-B05-339074	3
Fagron	Cholesterol		1
Fagron	Cholesterol	13F10-B40	1

- 111 117 spectra from 742 *Apo-Ident* customers from a total of 31 816 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cholesterol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all

relevant spectra of the various substances were compared with *Cholesterol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	120	0	119 022
Type C	0	129	1	111 117

The substance/substance group *Cholesterol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.2308 % (> 96.9231 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cholesterol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prasterone	19.10	—
Wool alcohols	35.71	—
Testosterone	43.28	—
Norethisterone acetate	46.07	—
Magnesium stearate	47.74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cholesterol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21219	23760	3.42	25.42
22461	22461	0.00	25.25
22971	23760	10.45	26.35
23760	23760	0.00	24.90
23937	23760	12.37	25.34

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Choline chloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22639-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Choline chloride; Cholinii chloridum

Special notes

When selecting the *Choline chloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Choline chloride	3	2	0

Second-stage model

For differentiation of the substance/substance group *Choline chloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Choline chloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Choline chloride	162092	22639	40	20160801*
Caelo	Choline chloride	14273819	22663	40	20141002
Caelo	Choline chloride	14273819	22734	40	20141002
Caelo	Choline chloride	16209209	23582	40	20160801

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Choline chloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Choline chloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Choline chloride	172053	23618	40
Caelo	Choline chloride	181082	24264	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Choline chloride*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Choline chloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Choline chloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	80	0	119 062
Type C	0	0	0	111 247

The substance/substance group *Choline chloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Choline chloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	84.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Choline chloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22639	22639	0.00	89.92
22663	22639	9.21	90.23
22734	22639	9.18	90.19
23582	22639	5.45	90.14

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Choline hydrogen tartrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20719-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Choline hydrogen tartrate; Cholinium bitartaricum

Special notes

When selecting the *Choline hydrogen tartrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Choline hydrogen tartrate	6	5	4

Second-stage model

For differentiation of the substance/substance group *Choline hydrogen tartrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Choline hydrogen tartrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Choline hydrogen...	1603044	22549	40	20160429*
Euro OTC	Choline hydrogen...	1607020	22689	40	20160808*
Euro OTC	Choline hydrogen...	1603044-01	23010	40	20160429
Euro OTC	Choline hydrogen...	1603044-01	23101	40	20160429
Euro OTC	Choline hydrogen...	1702005	23130	40	20170307*
Euro OTC	Choline hydrogen...	1901053	24484	40	20190228*
Euro OTC	Choline hydrogen...	1910013	24922	40	20191107*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Choline hydrogen tartrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Choline hydrogen tartrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Choline hydrogen tartrate	L1208016-01	20719	40
Euro OTC	Choline hydrogen tartrate	L1208016-02	21242	40
Euro OTC	Choline hydrogen tartrate	1707023	23610	40
Euro OTC	Choline hydrogen tartrate	1711022	23903	40
Euro OTC	Choline hydrogen tartrate	1802008	23958	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 7 spectra from 3 *Apo-Ident* customers from 5 batches from the substance/substance group *Choline hydrogen tartrate*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Choline hydrogen tartrate	1707023-01	1
Euro OTC	Choline hydrogen tartrate	1711022-01	1
Euro OTC	Choline hydrogen tartrate	1309023-01	2
Euro OTC	Choline hydrogen tartrate	1607020-01	2
Euro OTC	Choline hydrogen tartrate	1603044-01	1

- 111 240 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Choline hydrogen tartrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Choline hydrogen tartrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	200	0	118 942
Type C	0	7	0	111 240

The substance/substance group *Choline hydrogen tartrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Choline hydrogen tartrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Serine	57.77	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Choline hydrogen tartrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22549	22549	0.00	77.19
22689	22689	0.00	77.08
23010	22549	2.03	74.58
23101	22549	1.99	75.63
23130	23130	0.00	64.79
24484	24484	0.00	73.69
24922	24922	0.00	68.52

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ciclopirox olamine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20601-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ciclopirox olamine; Ciclopirox olaminum

Special notes

When selecting the *Ciclopirox olamine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ciclopirox olamine	7	3	52

Second-stage model

For differentiation of the substance/substance group *Ciclopirox olamine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ciclopirox olamine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ciclopirox olamine	13343209	21298	40	AR-15-FG-016214-01
Caelo	Ciclopirox olamine	14147406	21655	60	AR-15-FG-014857-01
Caelo	Ciclopirox olamine	14147406	21655SI	60	AR-15-FG-014857-01
Caelo	Ciclopirox olamine	14378809	21991	60	20150227
Caelo	Ciclopirox olamine	14378809	21991SI	60	20150227
Caelo	Ciclopirox olamine	15364408	23011	40	20151201
Caelo	Ciclopirox olamine	15364408	23011SI	40	20151201
Fagron	Ciclopirox olamine	13A16-N04	21218	40	20130117
Fagron	Ciclopirox olamine	14F13-B03-302340	21964	60	1608170
Fagron	Ciclopirox olamine	14F13-B03-302340	21964SI	60	1608170
Fagron	Ciclopirox olamine	16G26-B02-324884	22969	40	20160907
Fagron	Ciclopirox olamine	16G26-B02-324884	23108	40	20160907

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 600 spectra of 12 reference samples from the substance/substance group *Ciclopirox olamine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 089 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 6 reference samples from the substance/substance group *Ciclopirox olamine*.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ciclopirox olamine	12040906	20648	40
Caelo	Ciclopirox olamine	182102	24280	40
Fagron	Ciclopirox olamine	14E21-M04	21594	60
Fagron	Ciclopirox olamine	14E21-M04	21594SI	60
Fagron	Ciclopirox olamine	16G26-B02-324884	22969SI [†]	40
Fagron	Ciclopirox olamine	16G26-B02-324884	23108SI [†]	40

- 118 862 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 131 spectra from 71 *Apo-Ident* customers from 55 batches from the substance/substance group *Ciclopirox olamine*.
- Among them are spectra of independent samples from 52 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Ciclopirox olamine	17118806	1
Cael	Ciclopirox olamine	12040911	2
Caelo	Ciclopirox olamine	13343208	2
Caelo	Ciclopirox olamine	14147405	1
Caelo	Ciclopirox olamine	14275802	2
Caelo	Ciclopirox olamine	14275801	2
Caelo	Ciclopirox olamine	14378801	2
Caelo	Ciclopirox olamine	15018803	1
Caelo	Ciclopirox olamine	14378803	1
Caelo	Ciclopirox olamine	14378805	2
Caelo	Ciclopirox olamine	14378810	6
Caelo	Ciclopirox olamine	14378802	1
Caelo	Ciclopirox olamine	15364404	2
Caelo	Ciclopirox olamine	15364407	4
Caelo	Ciclopirox olamine	15364409	1
Caelo	Ciclopirox olamine	15364412	5
Caelo	Ciclopirox olamine	13343201	1
Caelo	Ciclopirox olamine	15304407	1
Caelo	Ciclopirox olamine	15364416	2
Caelo	Ciclopirox olamine	17118806	9
Caelo	Ciclopirox olamine	17118808	4
Caelo	Ciclopirox olamine	16G26-B02-337355	1
Caelo	Ciclopirox olamine	17307405	2

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Ciclopirox olamine	17307408	1
Caelo	Ciclopirox olamine	18210201	4
Caelo	Ciclopirox olamine	17118811	4
Caelo	Ciclopirox olamine	12040911	1
Caelo	Ciclopirox olamine	15364405	3
Caelo	Ciclopirox olamine	12040906	1
Caelo	Ciclopirox olamine	18210210	1
Caelo	Ciclopirox olamine	173074055727	1
Caelo	Ciclopirox olamine	15364402	2
Caelo	Ciclopirox olamine	14147402	4
Caelo	Ciclopirox olamine	17118801	2
Caelo	Ciclopirox olamine	13343203	1
Caelo	Ciclopirox olamine	14378806	5
Caelo	Ciclopirox olamine	17118802	3
Caelo	Ciclopirox olamine	17118807	2
Caelo	Ciclopirox olamine	18210202	2
Caelo	Ciclopirox olamine	17307402	3
Caelo	Ciclopirox olamine	13343	1
Caelo	Ciclopirox olamine	17307410	3
Caesar & Lorenz GmbH	Ciclopirox olamine	171188007	1
Caesar & Loretz GmbH	Ciclopirox olamine	17307410	1
Cealo	Ciclopirox olamine	14147403	2
Fagron	Ciclopirox olamine	10L09-N03	1
Fagron	Ciclopirox olamine	12G12-N09	2
Fagron	Ciclopirox olamine	14F13-B03-302339	1
Fagron	Ciclopirox olamine	A160013	1
Fagron	Ciclopirox olamine	14E21-M05	1
Fagron	Ciclopirox olamine	11h03-n02	1
Gehe	Ciclopirox olamine	14E21-M04	1
GEHE	Ciclopirox olamine	15364405	1
Noweda	Ciclopirox olamine	12B22-N03	1
Noweda	Ciclopirox olamine	12040911	1
Euro OTC	Ciclopirox olamine	1718806	1
Pharmachem	Ciclopirox olamine	17118808	1
Phoenix	Ciclopirox olamine	15364412	1
Phönix	Ciclopirox olamine	13A16-N04	1
Sanacorp	Ciclopirox olamine	17118806	1
Caelo	Ciclopirox olamine	15018802	3
Caelo	Ciclopirox olamine	12B22-N03	1
Caelo	Ciclopirox olamine	13343209	3
Caelo	Ciclopirox olamine	15364408	4
Fagron	Ciclopirox olamine	13A16-N04	1

- 111 116 spectra from 742 *Apo-Ident* customers from a total of 31 836 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ciclopirox olamine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ciclopirox olamine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	600	0	110 089
Type B	0	280	0	118 862
Type C	0	124	7	111 116

The substance/substance group *Ciclopirox olamine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	94.6565 % (> 92.3664 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ciclopirox olamine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ornithine aspartate	68.45	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ciclopirox olamine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21298	21298	0.00	82.46
21991	21298	3.78	81.52
21218	21964	5.03	73.81
21964	21964	0.00	68.45
22969	21964	5.31	76.72
23108	21964	4.80	74.26
23011	21298	3.88	82.61
21655	21655	0.00	85.96

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ciclosporin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20941-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ciclosporin; Ciclosporinum

Special notes

When selecting the *Ciclosporin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ciclosporin	4	4	62

Second-stage model

For differentiation of the substance/substance group *Ciclosporin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ciclosporin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ciclosporin	13148604	21474	60	1412541
Caelo	Ciclosporin	13148604	21475	60	20130613
Caelo	Ciclosporin	173327	24401	35	20180111*
Fagron	Ciclosporin	13D26-N07	20941	40	1402057
Fagron	Ciclosporin	13D26-N07	21671	42	1508429
Fagron	Ciclosporin	18G30_B04-354759	24441	40	20181115

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 277 spectra of 6 reference samples from the substance/substance group *Ciclosporin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 412 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 163 spectra of 6 reference samples from the substance/substance group *Ciclosporin*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ciclosporin	12317707	21082	30
Caelo	Ciclosporin	15278907	22966	40
Caelo	Ciclosporin	171583	23669	40
Fagron	Ciclosporin	16C09-B02-325955	23521	30
Caelo	Ciclosporin	173327	24401 [†]	5
Fagron	Ciclosporin	13D26-N07	21671 [†]	18

- 118 979 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 181 spectra from 76 *Apo-Ident* customers from 67 batches from the substance/substance group *Ciclosporin*.
- Among them are spectra of independent samples from 62 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Ciclosporin	19011301	1
Caelo	Ciclosporin	13031303	1
Caelo	Ciclosporin	12317702	2
Caelo	Ciclosporin	12317707	4
Caelo	Ciclosporin	13148606	6
Caelo	Ciclosporin	14A15-No1	1
Caelo	Ciclosporin	13346803	3
Caelo	Ciclosporin	14199104	3
Caelo	Ciclosporin	15278904	4
Caelo	Ciclosporin	15278910	1
Caelo	Ciclosporin	15278913	1
Caelo	Ciclosporin	17158306	3
Caelo	Ciclosporin	17158309	2
Caelo	Ciclosporin	13031801	1
Caelo	Ciclosporin	18041817	1
Caelo	Ciclosporin	18136101	3
Caelo	Ciclosporin	18136104	3
Caelo	Ciclosporin	15278902	2
Caelo	Ciclosporin	17332702	5
Caelo	Ciclosporin	19055804	11
Caelo	Ciclosporin	19055805	3
Caelo	Ciclosporin	15049703	3
Caelo	Ciclosporin	13346808	1
Caelo	Ciclosporin	12165603	2
Caelo	Ciclosporin	1733702	1
Caelo	Ciclosporin	18136108	3
Caelo	Ciclosporin	15278901	3
Caelo	Ciclosporin	13D26-N07	4

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Ciclosporin	29689114C22B02	1
Caelo	Ciclosporin	17158303	4
Caelo	Ciclosporin	17332703	2
Caelo	Ciclosporin	12165602	3
Caelo	Ciclosporin	13A28-N04	4
Caelo	Ciclosporin	15278903	3
Caesar & Loretz GmbH	Ciclosporin	18136104	4
Caesar & Loretz GmbH	Ciclosporin	19055804	1
Concord Biotech Ltd./ N...	Ciclosporin	14G22-B02-296891	1
Fagron	Ciclosporin	12E31-N02	7
Fagron	Ciclosporin	11K17-N13	1
Fagron	Ciclosporin	13A28-n04	1
Fagron	Ciclosporin	13A28-N04	4
Fagron	Ciclosporin	25051302	1
Fagron	Ciclosporin	1103531	1
Fagron	Ciclosporin	13B19-N02	3
Fagron	Ciclosporin	13B19N02	2
Fagron	Ciclosporin	13H19-N09	4
Fagron	Ciclosporin	16121401	1
Fagron	Ciclosporin	14G22-B02-296891	5
Fagron	Ciclosporin	14/18-B02-300180	1
Fagron	Ciclosporin	13414038	1
Fagron	Ciclosporin	15D23-B05	2
Fagron	Ciclosporin	15f29-b14-316270	2
Fagron	Ciclosporin	15D23-B05-308853	5
Fagron	Ciclosporin	15F29-B14-316270	1
Fagron	Ciclosporin	14g22-b02-296891	1
Fagron	Ciclosporin	13417083	1
Fagron	Ciclosporin	18A18-B07-344620	2
Fagron	Ciclosporin	15F29B14316270	1
Fagron	Ciclosporin	18136104	1
Fagron	Ciclosporin	15D23-B05-307217	1
Fagron	Ciclosporin	15f29-b14-325654	1
Fagron	Ciclosporin	15F29-B14	1
Fagron	Ciclosporin	18G30-B04-354759	1
Fagron	Ciclosporin	13H19_N09	1
Fagron	Ciclosporin	14718-b02-300180	1
Fagron	Ciclosporin	14a15-n01	1
Fagron	Ciclosporin	10J18-N06	1
Fargon	Ciclosporin	13D26-No7	1
Gehe	Ciclosporin	17158303	1
Gehe	Ciclosporin	17158306	1
Gehe	Ciclosporin	17332702	1
Gehe	Ciclosporin	17332703	1
Gehe	Ciclosporin	18136101	1
Fagron	Ciclosporin	13d026N07	1
Phoenix	Ciclosporin	17158303	1
Fagron	Ciclosporin	14A15-N01	3
Phönix	Ciclosporin	13D26-N07	1
Caelo	Ciclosporin	12317703	1
VDL	Ciclosporin	13D26-N07	1
Caelo	Ciclosporin	13148604	2
Fagron	Ciclosporin	13D26-N07	8

- 111 066 spectra from 742 *Apo-Ident* customers from a total of 31 825 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ciclosporin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ciclosporin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	277	0	110 412
Type B	0	132	31	118 979
Type C	0	143	38	111 066

The substance/substance group *Ciclosporin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8339 %)
Type B	100.0000 % (> 99.9893 %)	80.9816 % (> 79.1411 %)
Type C	100.0000 % (> 99.8899 %)	79.0055 % (> 77.3481 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ciclosporin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Erythromycin	22.73	—
Betamethasone valerate	26.26	—
Budesonide, micronized	26.87	—
Dexamethasone	28.45	—
Estradiol valerate	35.56	—
Prednisolon dihydrogen phosphate dinat...	37.07	—
Triamcinolone acetonide	45.58	—
Dexamethasone acetate	45.76	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ciclosporin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21671	21671	0.00	22.73
24441	21474	5.17	27.50
20941	20941	0.00	27.05
21474	21474	0.00	26.66
21475	21474	0.53	26.26
24401	24401	0.00	25.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ciprofloxacin hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20945-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ciprofloxacin hydrochloride; Ciprofloxacin hydrochloridum

Special notes

When selecting the *Ciprofloxacin hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ciprofloxacin hydrochloride	3	3	8

Second-stage model

For differentiation of the substance/substance group *Ciprofloxacin hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ciprofloxacin hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ciprofloxacin hy...	12B08-N03	20945	40	1401421
Fagron	Ciprofloxacin hy...	14B25-B02	21254	40	20140324
Fagron	Ciprofloxacin hy...	18F27-B01-353346	24581	40	20180814

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Ciprofloxacin hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Ciprofloxacin hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ciprofloxacin hydrochloride	15D07-B01-312864	22755	40
Fagron	Ciprofloxacin hydrochloride	16B17-B05-341882	23938	40
Fagron	Ciprofloxacin hydrochloride	17K09-B02-345976	23991	40

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Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ciprofloxacin hydrochloride	15D07-B01-312864	23568	40

- 118 982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 9 spectra from 6 *Apo-Ident* customers from 8 batches from the substance/substance group *Ciprofloxacin hydrochloride*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Ciprofloxacin hydrochloride	16B17-B05-324218	1
Fagron	Ciprofloxacin hydrochloride	14B25-B02-291-783	1
Fagron	Ciprofloxacin hydrochloride	15D07-B01-312864	1
Fagron	Ciprofloxacin hydrochloride	14B25-B02-291783	2
Fagron	Ciprofloxacin hydrochloride	14I15-B08	1
Fagron	Ciprofloxacin hydrochloride	14/15-B08-303363	1
Fagron	Ciprofloxacin hydrochloride	14I15-B08	1
Fagron	Ciprofloxacin hydrochloride	14I15-B08-303363	1

- 111 238 spectra from 742 *Apo-Ident* customers from a total of 31 883 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ciprofloxacin hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ciprofloxacin hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	160	0	118 982
Type C	0	9	0	111 238

The substance/substance group *Ciprofloxacin hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ciprofloxacin hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	45.56	–
Eosin Y	54.44	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ciprofloxacin hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20945	20945	0.00	67.40
21254	20945	9.11	68.89
24581	20945	14.23	68.49

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Citric acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20019-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Citric acid; Acidum citricum

Special notes

When selecting the *Citric acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Citric acid	7	11	439

Second-stage model

For differentiation of the substance/substance group *Citric acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Citric acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Citric acid	11380204	20682	40	20120127
Caelo	Citric acid	12043112	20683	40	20120229
Caelo	Citric acid	13396502	21455	60	20140110
Caelo	Citric acid	13243213	21487	40	20130821
Caelo	Citric acid	160386	22463	60	20160315*
Fagron	Citric acid	12F18-N03	20706	40	20120628
Fagron	Citric acid	13G24-N13	20913	40	20130827

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Citric acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 369 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 540 spectra of 13 reference samples from the substance/substance group *Citric acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Citric acid	160387	22478	60
Caelo	Citric acid	162086	22620	40
Caelo	Citric acid	162154	22622	40
Caelo	Citric acid	171627	23303	40
Caelo	Citric acid	171626	23421	40
Caelo	Citric acid	180976	24034	40
Caelo	Citric acid	181292	24232	40
Caelo	Citric acid	183121	24366	40
Caelo	Citric acid	183071	24367	40
Caelo	Citric acid	192036	24740	40
Caelo	Citric acid	192073	24744	40
Caelo	Citric acid	171626	23648	40
Caelo	Citric acid	171627	23677	40

- 118602 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2179 spectra from 588 *Apo-Ident* customers from 455 batches from the substance/substance group *Citric acid*.
- Among them are spectra of independent samples from 437 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
12.12.2016 Phoenix 4,59EUR	Citric acid	15088008	1
A.H. 08.06.13 ek: 6,92EUR	Citric acid	13050604	1
AHD	Citric acid	13050607	1
AHD	Citric acid	13396502	1
AHD	Citric acid	15063218	1
AHD	Citric acid	17329511	1
ALH	Citric acid	L1508013-01	1
Fagron	Citric acid	14E06-B07293872	1
Alliance Health 03.06.2...	Citric acid	13K18-B34	1
Alliance Healthcare	Citric acid	12043123	1
anzag	Citric acid	13175409	1
Anzag	Citric acid	10049712	1
Anzag	Citric acid	10049713	1
Anzag	Citric acid	6494061	1
Audor Pharma	Citric acid	PA201	1
Fagron	Citric acid	14k05-b04-302816	1
Beyvers	Citric acid	16038606	1
Bombastus	Citric acid	13396502	1
Bombastus	Citric acid	272757	2
Bombastus	Citric acid	17162601	2

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Supplier	Substance	Batch	Spectra
Bombastus	Citric acid	17162602	1
Caelo	Citric acid	12043118	3
Caelo	Citric acid	9158408	1
Caelo	Citric acid	11159801	2
Caelo	Citric acid	11178303	5
Caelo	Citric acid	11189817	1
Caelo	Citric acid	12043123	6
Caelo	Citric acid	9199105	1
Caelo	Citric acid	12156801	2
Caelo	Citric acid	10049716	1
Caelo	Citric acid	1380208	1
Caelo	Citric acid	20151112-1	1
Caelo	Citric acid	20060912-3	1
Caelo	Citric acid	11C24-N02	1
Caelo	Citric acid	11066806	1
Caelo	Citric acid	12156803	8
Caelo	Citric acid	12043124	3
Caelo	Citric acid	12156811	11
Caelo	Citric acid	713I-01024	1
Caelo	Citric acid	11159821	1
Caelo	Citric acid	12B01-N01	5
Caelo	Citric acid	11380215	3
Caelo	Citric acid	12156827	1
Caelo	Citric acid	19041305	1
Caelo	Citric acid	19041304	1
Caelo	Citric acid	13050604	13
Caelo	Citric acid	12156818	1
Caelo	Citric acid	11159817	1
Caelo	Citric acid	13050607	9
Caelo	Citric acid	A-040513-1	1
Caelo	Citric acid	13050601	9
Caelo	Citric acid	12156832	7
Caelo	Citric acid	12156824	5
Caelo	Citric acid	12156830	1
Caelo	Citric acid	11380213	1
Caelo	Citric acid	2071303	1
Caelo	Citric acid	13050614	7
Caelo	Citric acid	13050610	6
Caelo	Citric acid	13050623	2
Caelo	Citric acid	17071301	1
Caelo	Citric acid	13050622	7
Caelo	Citric acid	12156822	2
Caelo	Citric acid	13175405	5
Caelo	Citric acid	11380217	2
Caelo	Citric acid	10182420	1
Caelo	Citric acid	27091303	1
Caelo	Citric acid	13175411	10
Caelo	Citric acid	26111301	1
Caelo	Citric acid	13157404	1
Caelo	Citric acid	13175403	14
Caelo	Citric acid	12175711	1
Caelo	Citric acid	L130404202	1
Caelo	Citric acid	13175414	2
Caelo	Citric acid	28021405	1
Caelo	Citric acid	13243201	17
Caelo	Citric acid	13243202	10
Caelo	Citric acid	13175410	4
Caelo	Citric acid	12175718	1
Caelo	Citric acid	28051401	1
Caelo	Citric acid	13243219	4

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Supplier	Substance	Batch	Spectra
Caelo	Citric acid	13243220	2
Caelo	Citric acid	13243218	9
Caelo	Citric acid	12353613	1
Caelo	Citric acid	13396504	3
Caelo	Citric acid	15091401	1
Caelo	Citric acid	18091409	1
Caelo	Citric acid	13K18-B34-291520	1
Caelo	Citric acid	13396505	2
Caelo	Citric acid	13243216	11
Caelo	Citric acid	24021502	1
Caelo	Citric acid	13031502	1
Caelo	Citric acid	13396506	1
Caelo	Citric acid	14041506	1
Caelo	Citric acid	14186312	14
Caelo	Citric acid	14186301	22
Caelo	Citric acid	13243229	2
Caelo	Citric acid	13061502	1
Caelo	Citric acid	15044902	3
Caelo	Citric acid	1072015B	1
Caelo	Citric acid	15087510	1
Caelo	Citric acid	14071501	1
Caelo	Citric acid	15124301	9
Caelo	Citric acid	15063206	19
Caelo	Citric acid	15214301	1
Caelo	Citric acid	15087902	3
Caelo	Citric acid	15063211	5
Caelo	Citric acid	15063203	15
Caelo	Citric acid	15063202	1
Caelo	Citric acid	15087903	16
Caelo	Citric acid	15063204	9
Caelo	Citric acid	15124202	1
Caelo	Citric acid	15063218	11
Caelo	Citric acid	15063214	6
Caelo	Citric acid	2789	1
Caelo	Citric acid	1181765	1
Caelo	Citric acid	16038704	9
Caelo	Citric acid	150632	1
Caelo	Citric acid	160607AC	1
Caelo	Citric acid	16038613	9
Caelo	Citric acid	15124303	1
Caelo	Citric acid	xxxxxx	1
Caelo	Citric acid	xxxx	1
Caelo	Citric acid	16038621	13
Caelo	Citric acid	8031702	1
Caelo	Citric acid	16038709	5
Caelo	Citric acid	1516Q-01024	1
Caelo	Citric acid	1501-B06-324348	1
Caelo	Citric acid	15087904	1
Caelo	Citric acid	15G16-B01-330450	1
Caelo	Citric acid	2051703	1
Caelo	Citric acid	16038607	5
Caelo	Citric acid	16208607	26
Caelo	Citric acid	16208610	9
Caelo	Citric acid	15G16-B01-330449	2
Caelo	Citric acid	6071713	1
Caelo	Citric acid	26071701	1
Caelo	Citric acid	16208612	19
Caelo	Citric acid	16038712	5
Caelo	Citric acid	3091701	1
Caelo	Citric acid	16215408	3

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Supplier	Substance	Batch	Spectra
Caelo	Citric acid	18111704	1
Caelo	Citric acid	17162702	6
Caelo	Citric acid	17162603	5
Caelo	Citric acid	16215409	6
Caelo	Citric acid	13011801	1
Caelo	Citric acid	162086055525	1
Caelo	Citric acid	5041802	1
Caelo	Citric acid	18025704	14
Caelo	Citric acid	1716262601	1
Caelo	Citric acid	17329504	1
Caelo	Citric acid	17329503	2
Caelo	Citric acid	26051803	1
Caelo	Citric acid	17329511	6
Caelo	Citric acid	18097601	17
Caelo	Citric acid	17329513	2
Caelo	Citric acid	18129205	14
Caelo	Citric acid	18129206	2
Caelo	Citric acid	17E15-B04-339371	1
Caelo	Citric acid	17162706	1
Caelo	Citric acid	18097604	1
Caelo	Citric acid	18306906	19
Caelo	Citric acid	18306905	15
Caelo	Citric acid	18306909	14
Caelo	Citric acid	18307102	3
Caelo	Citric acid	18306911	8
Caelo	Citric acid	12175708	3
Caelo	Citric acid	18306903	7
Caelo	Citric acid	16208608	6
Caelo	Citric acid	16038707	9
Caelo	Citric acid	13396515	2
Caelo	Citric acid	15044905	10
Caelo	Citric acid	20170728/Ma1	1
Caelo	Citric acid	18025701	31
Caelo	Citric acid	162154	1
Caelo	Citric acid	170607C/16208605	1
Caelo	Citric acid	1812905	1
Caelo	Citric acid	16038604	9
Caelo	Citric acid	16004706	18
Caelo	Citric acid	14G04-B09	1
Caelo	Citric acid	1396505	1
Caelo	Citric acid	6498011	1
Caelo	Citric acid	13A04-N04	4
Caelo	Citric acid	15063006	5
Caelo	Citric acid	11159824	1
Caelo	Citric acid	13175409	20
Caelo	Citric acid	16038622	6
Caelo	Citric acid	18097611	3
Caelo	Citric acid	18306908	1
Caelo	Citric acid	L1609021-01	3
Caelo	Citric acid	11C24-N03	1
Caelo	Citric acid	12175717	1
Caelo	Citric acid	13050613	18
Caelo	Citric acid	15044903	5
Caelo	Citric acid	1155609	2
Caelo	Citric acid	133243218	1
Caelo	Citric acid	16208613	10
Caelo	Citric acid	13050617	12
Caelo	Citric acid	13050621	2
Caelo	Citric acid	13243217	6
Caelo	Citric acid	15063003-20160615Ma1	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Citric acid	13050606	2
Caelo	Citric acid	5315I-01024	1
Caelo	Citric acid	L1508013-01	1
Caelo	Citric acid	15044904	10
Caelo	Citric acid	16004701	19
Caelo	Citric acid	15063213	23
Caelo	Citric acid	1716271	1
Caelo	Citric acid	18129207	1
Caelo	Citric acid	18129204	1
Caelo	Citric acid	3275	1
Caelo	Citric acid	1172673	1
Caelo	Citric acid	1917A-01024	1
Caelo	Citric acid	2317M-01024	1
Caelo	Citric acid	12043113	3
Caelo	Citric acid	13D29-N02	1
Caelo	Citric acid	12156812	4
Caelo	Citric acid	13243210	9
Caelo	Citric acid	16208614	36
Caelo	Citric acid	16038602	3
Caelo	Citric acid	15088016	4
Caelo	Citric acid	15088017	2
Caelo	Citric acid	13175404	4
Caelo	Citric acid	12043119	1
Caelo	Citric acid	16004702	25
Caelo	Citric acid	1015U-01024	1
Caelo	Citric acid	18312104	4
Caelo	Citric acid	11K07-N01	1
Caelo	Citric acid	18025802	6
Caelo	Citric acid	13243224	2
Caelo	Citric acid	16208615	3
Caelo	Citric acid	14186313	9
Caelo	Citric acid	16038608	14
Caelo	Citric acid	11380208	1
Caelo	Citric acid	13G24-N13	4
Caelo	Citric acid	13175406	3
Caelo	Citric acid	13243214	15
Caelo	Citric acid	13243221	8
Caelo	Citric acid	13K18-B34-288372	1
Caelo	Citric acid	14186302	14
Caelo	Citric acid	15063205	3
Caelo	Citric acid	16038603	5
Caelo	Citric acid	15063217	10
Caelo	Citric acid	21531	1
Caelo	Citric acid	7808	1
Caelo	Citric acid	1150817/16208614	1
Caelo	Citric acid	17162602	20
Caelo	Citric acid	17329502	12
Caelo	Citric acid	18097610	1
Caelo	Citric acid	15088008	2
Caelo	Citric acid	13050618	3
Caelo	Citric acid	16038606	19
Caelo	Citric acid	12043105	2
Caelo	Citric acid	12043110	4
Caelo	Citric acid	1305601	1
Caelo	Citric acid	13243225	4
Caelo	Citric acid	13243005	1
Caelo	Citric acid	13243222	1
Caelo	Citric acid	jjjjjj	1
Caelo	Citric acid	16038701	5
Caelo	Citric acid	2716A-01024	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Citric acid	17162701	22
Caelo	Citric acid	16206813	1
Caelo	Citric acid	17162601	24
Caelo	Citric acid	18025702	42
Caelo	Citric acid	17161601	1
Caelo	Citric acid	18097602	4
Caelo	Citric acid	16215405	4
Caelo	Citric acid	160614	1
Caelo	Citric acid	13K18-B34-291522	1
Caelo	Citric acid	14G04-B09-293874	2
Caelo	Citric acid	16038617	2
Caelo	Citric acid	13K18-B34-288371TEST	1
Caelo	Citric acid	13K18-B34	1
Caelo	Citric acid	13K18-B34-291523	2
Caelo	Citric acid	14G04B09293877	1
Caelo	Citric acid	14K05-B04-302815	1
Caelo	Citric acid	16038708	9
Caelo	Citric acid	16208606	24
Caelo	Citric acid	16215403	3
Caelo	Citric acid	2617Q-01024	1
Caelo	Citric acid	1620610	1
Caelo	Citric acid	180257004	1
Caelo	Citric acid	18097609	12
Caelo	Citric acid	18097607	5
Caelo	Citric acid	14186314	4
Caelo	Citric acid	15063003	22
Caelo	Citric acid	180257045617	1
Caelo	Citric acid	18307104	1
Caelo	Citric acid	12156804	3
Caelo	Citric acid	121568704	1
Caelo	Citric acid	13050611	6
Caelo	Citric acid	13050623-3376319052	1
Caelo	Citric acid	13243208	2
Caelo	Citric acid	1175409	2
Caelo	Citric acid	15044901	8
Caelo	Citric acid	14E06-B07	1
Caelo	Citric acid	1044905	1
Caelo	Citric acid	16004705	4
Caelo	Citric acid	16038614	4
Caelo	Citric acid	18025801	20
Caelo	Citric acid	17162604	3
Caelo	Citric acid	17329512	2
Caelo	Citric acid	18097606	10
Caelo	Citric acid	18306902	23
Caeolo/Gehe	Citric acid	15044903	3
Caesar & Lorenz GmbH	Citric acid	16004706	1
Caesar & Loretz	Citric acid	15087904	2
Caesar & Loretz GmbH	Citric acid	13243201	1
Caesar & Loretz GmbH	Citric acid	13243214	1
Caesar & Loretz GmbH	Citric acid	15063003	2
Caesar & Loretz GmbH	Citric acid	15063203	1
Caesar & Loretz GmbH	Citric acid	16208614	1
Caesar & Loretz GmbH	Citric acid	18306902	1
Caesar & Loretz GmbH	Citric acid	18129205	1
Caesar & Loretz GmbH	Citric acid	18F25-B02	1
Caesar & Loretz GmbH	Citric acid	18F25-B02_351454	1
Caesar & Loretz GmbH	Citric acid	18097606	1
Caesar & Loretz GmbH	Citric acid	18306905	4
Caesar & Loretz GmbH	Citric acid	18129207	1
Caesar & Loretz GmbH	Citric acid	18306903	4

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continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Citric acid	18306906	4
Caesar & Loretz GmbH	Citric acid	18306909	3
Caesar & Loretz GmbH	Citric acid	18312104	2
Caesar & Loretz GmbH	Citric acid	18306904	1
Caesar & Loretz GmbH	Citric acid	18306911	1
Caesar & Loretz GmbH / ...	Citric acid	15063203	1
Caesar & Loretz GmbH / ...	Citric acid	16208614	1
Caesar & Loretz GmbH / ...	Citric acid	18306906	1
Caesar & Loretz GmbH / ...	Citric acid	18025702	1
Caesar & Loretz GmbH / ...	Citric acid	18097609	2
Caesar & Loretz GmbH/Kr...	Citric acid	18306909	1
Caesar & Loretz GmbH/Kr...	Citric acid	18306911	1
Caesar & Loretz GmbH/No...	Citric acid	18306908	1
Caesar & Loretz GmbH/Ph...	Citric acid	18097606	1
Caesar & Loretz GmbH/Ph...	Citric acid	192073002	1
Caesar & Loretz/ Noweda	Citric acid	12156812	1
Caesar&Loretz GmbH	Citric acid	15063213	1
Caesar&Loretz GmbH	Citric acid	16038604	1
Caesar&Loretz GmbH,16.0...	Citric acid	16004706	1
Caesar&lorenz,Phoenix	Citric acid	13243201	1
Caesar/Lorenz	Citric acid	13050610	1
Caolo- Noweda	Citric acid	15063213	1
Cealo/AHD	Citric acid	16038704	1
Cealo/Anzag	Citric acid	16208607	1
Cealo/Gehe	Citric acid	14186301	6
Cordes/Noweda	Citric acid	16208607	1
E Plus	Citric acid	16208613	1
Ebert & Jacobi 12.07...	Citric acid	1506214	1
Ebert-Jacobi	Citric acid	16208607	1
Eu Rho	Citric acid	L1202001-01	1
EuRho	Citric acid	L1503027-02	2
EuRho/Alliance Healthcare	Citric acid	L1609021-02	1
euro / Phoenix 19.02.2018	Citric acid	L1609021	1
Euro OTC	Citric acid	13K18-B34	1
Euro OTC	Citric acid	L1202001-01	5
Euro OTC	Citric acid	L130404201	2
Euro OTC	Citric acid	L1304042-02	1
Euro OTC	Citric acid	13396515	1
Euro OTC	Citric acid	702260	4
Euro OTC	Citric acid	L1503027-02	3
Euro OTC	Citric acid	L1508013-02	1
Euro OTC	Citric acid	L1609021-02	3
Euro OTC	Citric acid	13175410	1
Euro OTC	Citric acid	L1408011-01	1
Euro OTC	Citric acid	1505029B	1
Euro OTC	Citric acid	L1609021-01	4
Euro OTC	Citric acid	1011047-03	2
Euro OTC	Citric acid	L1202001-02	1
Euro OTC	Citric acid	L1805017-01	1
Euro OTC	Citric acid	11604062-01	1
Euro OTC	Citric acid	1406014-02	1
Euro OTC	Citric acid	L1503027-01	1
Euro OTC	Citric acid	L1508013-01	3
Euro OTC	Citric acid	L1408011-02	2
Fagron	Citric acid	12B01-N01	1
Fagron	Citric acid	13804-N02	1
Fagron	Citric acid	1172673	10
Fagron	Citric acid	20071203	1
Fagron	Citric acid	700309-001	1
Fagron	Citric acid	11K07N01	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Citric acid	12B01-N01	23
Fagron	Citric acid	1913A-01024	1
Fagron	Citric acid	13A04-N04	13
Fagron	Citric acid	13A04-N04	1
Fagron	Citric acid	12B01N01	1
Fagron	Citric acid	13B04-N01	1
Fagron	Citric acid	26082013B	1
Fagron	Citric acid	probe	1
Fagron	Citric acid	13G24-N24	12
Fagron	Citric acid	700309-0006	1
Fagron	Citric acid	28021404	1
Fagron	Citric acid	22031401	1
Fagron	Citric acid	13K18-B34-288372	7
Fagron	Citric acid	16072014B	1
Fagron	Citric acid	13K18-B34-293871	2
Fagron	Citric acid	13F12-N08	1
Fagron	Citric acid	13L18-B39-289347	4
Fagron	Citric acid	14E06-B07-293875	3
Fagron	Citric acid	13G24N13	2
Fagron	Citric acid	13L05-B02-296246	3
Fagron	Citric acid	14E-06-B07-293890	1
Fagron	Citric acid	14G04-b09-293876	1
Fagron	Citric acid	1181765	3
Fagron	Citric acid	14G04-B09-293876	4
Fagron	Citric acid	11K11-N020444/1975	1
Fagron	Citric acid	14g04-b09293877	1
Fagron	Citric acid	13L05-B02-309050	1
Fagron	Citric acid	14E06-B07293873	1
Fagron	Citric acid	13L05B02296247	1
Fagron	Citric acid	14G04-B09-309836	3
Fagron	Citric acid	14K05_B04_302815	1
Fagron	Citric acid	15G16-B01-330450	8
Fagron	Citric acid	330449	1
Fagron	Citric acid	15G16-B01330450	1
Fagron	Citric acid	15101-B06-324348	1
Fagron	Citric acid	15G16-B01330449	2
Fagron	Citric acid	17E15-B04-345678	2
Fagron	Citric acid	17E15-B04-347169	3
Fagron	Citric acid	351453	1
Fagron	Citric acid	18F25-B02-355298	1
Fagron	Citric acid	12175711	1
Fagron	Citric acid	11C24-N03	6
Fagron	Citric acid	10G21-N05	2
Fagron	Citric acid	11K11-N02	2
Fagron	Citric acid	15G16-B01	2
Fagron	Citric acid	11C24-N02	3
Fagron	Citric acid	11K07-N01	7
Fagron	Citric acid	13K18-B34-291522	3
Fagron	Citric acid	13K18-B34_291522	1
Fagron	Citric acid	13A-04-N04	2
Fagron	Citric acid	13A04N04	1
Fagron	Citric acid	15044902	1
Fagron	Citric acid	13K18-B34	5
Fagron	Citric acid	13K18-B34-291072	2
Fagron	Citric acid	1156158	1
Fagron	Citric acid	13F12-N01	3
Fagron	Citric acid	15g16-b01-330450	2
Fagron	Citric acid	13k18-b34-291522	1
Fagron	Citric acid	6496091	1
Fagron	Citric acid	12F06-M06	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Citric acid	13K18-B34-288373	1
Fagron	Citric acid	14G04-B09-293874	11
Fagron	Citric acid	12B01-N01	1
Fagron	Citric acid	214U-01024	1
Fagron	Citric acid	11H30-N05	1
Fagron	Citric acid	13K18-B34-291523	2
Fagron	Citric acid	14K05-B04-302816	6
Fagron	Citric acid	UJ501	2
Fagron	Citric acid	15G16b01	1
Fagron	Citric acid	13G24-N240739/900	1
Fagron	Citric acid	13G24-N240029/900	1
Fagron	Citric acid	14b06-b07-293872	1
Fagron	Citric acid	12801-N01	1
Fagron	Citric acid	13K18-B34-291071	4
Fagron	Citric acid	13G04-N05	5
Fagron	Citric acid	100614d	1
Fagron	Citric acid	16208607	1
Fagron	Citric acid	13A04-N040019/4900	1
Fagron	Citric acid	13K18-B34-288371	4
Fagron	Citric acid	14E06-B07-293872	3
Fagron	Citric acid	1714Q1024	1
Fagron	Citric acid	11C24N022869/4250	1
Fagron	Citric acid	15G16B01	1
Fagron	Citric acid	18F25-B02	1
Fagron	Citric acid	14K05-B04-302815	5
Fagron	Citric acid	4810E-01024	1
Fagron	Citric acid	13K18-B34-291519	5
Fagron	Citric acid	13k18-B34-288372	1
Fagron	Citric acid	14E06-B07-293890	3
Fagron	Citric acid	14G04B09293876	1
Fagron	Citric acid	14G04-B09-296361	1
Fagron	Citric acid	14K05-B04-302817	2
Fagron	Citric acid	15G16B01330450	1
Fagron	Citric acid	17E15-B04	2
Fagron	Citric acid	14G04-B09-293877	9
Fagron	Citric acid	1151608	2
Fagron	Citric acid	12b01-N01	1
fargon	Citric acid	13A04-N04	1
Fargon	Citric acid	12B01-N01	1
Fargon	Citric acid	12B01-NN01	1
Fiebig	Citric acid	13243201	1
Fiebig	Citric acid	14K05-B04-302815	1
Fiebig	Citric acid	15063204	1
Fiebig	Citric acid	17162702	1
Finze	Citric acid	12156812	2
Fischar	Citric acid	6493071	1
Fischar	Citric acid	649061	2
Fischar	Citric acid	6494061	2
Fischar	Citric acid	6498011	1
Fischer/Noweda	Citric acid	6496091	1
fishar	Citric acid	6494061	1
Fragon/Phoenix	Citric acid	14G04-B09-293976	1
Fragon/Phönix	Citric acid	18F25-B02-351463	1
Fragron/Noweda	Citric acid	15G16-B01-330449	1
Gehe	Citric acid	11C24-N03	2
Gehe	Citric acid	11C24-N02	1
Gehe	Citric acid	12043111	1
Gehe	Citric acid	11K07-N01	2
Gehe	Citric acid	13175404	1
Gehe	Citric acid	13175403	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Gehe	Citric acid	15087902	1
Gehe	Citric acid	15G16-B01-330450	1
Gehe	Citric acid	16038614	1
Gehe	Citric acid	17162603	1
Gehe	Citric acid	16004706	1
Gehe	Citric acid	17162601	2
Gehe	Citric acid	18097607	1
GEHE	Citric acid	16208606	1
GEHE	Citric acid	18097607	1
GEHE	Citric acid	18097611	1
GEHE 02.07.2014	Citric acid	13243217	1
Gehe 21-01-2019	Citric acid	18097609	1
Gehe Kassel, 22.05.2015	Citric acid	14E06-B07-293872	1
Caelo	Citric acid	1230616	1
Caelo	Citric acid	16038713	1
Gehe/Euro	Citric acid	160406-02	1
Gehe/Fragon	Citric acid	14G04B09293876	1
Klenk	Citric acid	12B01-N01	2
Hepart	Citric acid	16208614	1
Ichthyol Gesellschaft//...	Citric acid	16038618	1
Jenne	Citric acid	15063002	1
Caelo	Citric acid	18097603	15
Jungbunzlauer Ladenburg...	Citric acid	1156158	1
Jungbunzlauer Ladenburg...	Citric acid	1155609	1
Kehr	Citric acid	17162602	1
Caelo	Citric acid	15185320	1
L10	Citric acid	9494185	1
Caelo	Citric acid	16208605	14
Lamotte	Citric acid	15063213	1
Nachtestung-Verlängerung	Citric acid	278/18	1
Noweda	Citric acid	12043110	1
Noweda	Citric acid	L1202001-02	1
Noweda	Citric acid	13050601	1
Noweda	Citric acid	13050621	1
Noweda	Citric acid	13243216	1
Noweda	Citric acid	16004701	1
Noweda	Citric acid	15087902	2
Noweda	Citric acid	15063203	1
Noweda	Citric acid	16208606	3
Noweda	Citric acid	18097606	1
Noweda	Citric acid	18306903	1
Noweda	Citric acid	16208614	1
Noweda	Citric acid	18306906	1
Fagron	Citric acid	12B01-No1	1
Noweda 13.6.2019	Citric acid	18306905	2
Fagron	Citric acid	13K18-B34-291520	4
Fagron	Citric acid	13H22-N09	2
Euro OTC	Citric acid	L1604061-02	4
Otto Fischar	Citric acid	6494061	1
Otto Fischar GmbH&Co. KG	Citric acid	6494061	6
Otto Fischar GmbH&Co. KG	Citric acid	6496051	1
Otto Fischar GmbH/ Nowe...	Citric acid	6494061	1
Otto Fischer / Sana	Citric acid	6493071	1
Otto Fischer GmbH	Citric acid	6492061	1
Caelo	Citric acid	14G04-B09-293876	4
Phoenix	Citric acid	12b01-N01	1
Phoenix	Citric acid	13243202	1
Phoenix	Citric acid	1172673	1
Phoenix	Citric acid	13K18-B34-288372	1
Phoenix	Citric acid	18097603	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Phoenix	Citric acid	18025701	1
Phoenix	Citric acid	19B06-B02-191458	1
Phoenix	Citric acid	18306911	1
Phoenix 07.04.2014	Citric acid	13A04-N04	1
Phoenix 12.12.2016 4,59EUR	Citric acid	1508808	1
Phoenix 31.01.2019	Citric acid	18097607	1
phoenix 5.6.14	Citric acid	1172673	1
phönix	Citric acid	16038604	3
phönix	Citric acid	16208608	1
Phönix	Citric acid	1155609	1
Phönix	Citric acid	13A04-N04	1
Phönix	Citric acid	14186312	4
Phönix	Citric acid	15063213	1
Phönix	Citric acid	123456	1
Phönix	Citric acid	16215406	1
Phönix	Citric acid	18025704	1
Phönix	Citric acid	18097603	2
Phönix	Citric acid	18097601	1
Phönix Gotha	Citric acid	13050609	1
Phönix Gotha	Citric acid	13050618	1
Phönix Gotha	Citric acid	12B01-N012125/6000	1
Phönix Gotha	Citric acid	12B01-N011973/6000	1
Phönix Gotha	Citric acid	12B01-N012028/6000	1
Phönix Gotha	Citric acid	13A04-N040049-100	1
Fagron	Citric acid	15G16-B01-330449	11
Caelo	Citric acid	16038710	3
Caelo	Citric acid	18F25-B02	1
Caelo	Citric acid	18F25-B02-351453	1
Fagron	Citric acid	1155609	9
Fagron	Citric acid	14G04-B09-309707	1
Phönix/Gehe	Citric acid	16208614	1
Sanacorb;20.04.15; 7,45EUR	Citric acid	1375410	1
sanacorp	Citric acid	13396505	1
Sanacorp	Citric acid	12156811	1
Sanacorp	Citric acid	12156832	1
Sanacorp	Citric acid	1216832	1
Sanacorp	Citric acid	12156823	1
Sanacorp	Citric acid	12156824	1
Sanacorp	Citric acid	13050604	1
Sanacorp	Citric acid	13243214	1
Sanacorp	Citric acid	40/AKD2	1
Sanacorp	Citric acid	13K18-B34-291072	1
Sanacorp	Citric acid	41/AKD4	1
Sanacorp	Citric acid	16208608	1
Sanacorp	Citric acid	16208614	1
Sanacorp	Citric acid	17162601	1
Sanacorp	Citric acid	18097603	1
Sanacorp	Citric acid	18025702	1
Caelo	Citric acid	13175426	4
Caelo	Citric acid	11K11-N02	1
Caelo	Citric acid	13050624	1
SanacorpWE:15.02.2017 ...	Citric acid	15063203	1
SanacorpWE:30.01.2017 ...	Citric acid	16038707	1
Caelo	Citric acid	12175716	2
Spangropharm	Citric acid	13050611	3
Fagron	Citric acid	700309-0003	2
Caelo	Citric acid	12043120	5
Caelo	Citric acid	12156823	4
Caelo	Citric acid	13175402	3
Fagron	Citric acid	13K18-B34-291521	4

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Supplier	Substance	Batch	Spectra
VDL 16.03.15; 2,54EUR	Citric acid	13243201	1
VDL;23.6.14; 2.49EUR	Citric acid	13243213	1
Wolf Apotheke	Citric acid	58(18097609)	1
Caelo	Citric acid	11380204	5
Caelo	Citric acid	12043112	3
Caelo	Citric acid	13243213	20
Caelo	Citric acid	13396502	3
Caelo	Citric acid		4
Euro OTC	Citric acid		5
	Citric acid	13K18-B34-291523	1
Fagron	Citric acid	13G24-N13	6
Fagron	Citric acid		1
Fargon/Sanacorp	Citric acid		1
Merck	Citric acid		1

- 109 068 spectra from 741 *Apo-Ident* customers from a total of 31 447 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Citric acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Citric acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	540	0	118 602
Type C	0	2127	52	109 068

The substance/substance group *Citric acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8889 %)
Type C	100.0000 % (> 99.8899 %)	97.6136 % (> 97.4759 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Citric acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Potassium hydrogen tartrate	26.21	—
Neomycin sulfate	38.18	—
Sodium ascorbate	44.61	—
Levothyroxin sodium	55.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Citric acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20683	22463	1.25	35.16
20913	22463	3.30	33.70
21487	22463	3.80	38.67
22463	22463	0.00	34.92
20682	22463	10.30	38.49
20706	22463	10.04	38.04
21455	22463	10.14	39.58

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Citric acid monohydrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20012-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Citric acid monohydrate; Acidum citricum monohydricum

Special notes

When selecting the *Citric acid monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Citric acid monohydrate	6	1	70

Second-stage model

For differentiation of the substance/substance group *Citric acid monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Citric acid monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Citric acid mono...	15185301	22340	60	20150708
Caelo	Citric acid mono...	17085602	23409	40	20170410
Caelo	Citric acid mono...	181305	24222	40	20180606*
Fagron	Citric acid mono...	12D26-N02	20926	40	20120515
Hedinger	Citric acid mono...	202029	23457	40	20161110
Hedinger	Citric acid mono...	202029	23458	40	1908675
Hedinger	Citric acid mono...	202030	24874	40	20180727

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Citric acid monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 389 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Citric acid monohydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Citric acid monohydrate	161865	22617	40
Caelo	Citric acid monohydrate	161865	23298	40

- 119062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 219 spectra from 96 *Apo-Ident* customers from 73 batches from the substance/substance group *Citric acid monohydrate*.
- Among them are spectra of independent samples from 70 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance Healthcare	Citric acid monohydrate	18130503	1
Bombastus	Citric acid monohydrate	259437	1
Bombastus	Citric acid monohydrate	309343	1
Bombastus	Citric acid monohydrate	309344	2
Bombastus	Citric acid monohydrate	309650	1
Bombastus	Citric acid monohydrate	70620101	1
Bombastus	Citric acid monohydrate	294630	1
Caelo	Citric acid monohydrate	13069104	6
Caelo	Citric acid monohydrate	1212937	1
Caelo	Citric acid monohydrate	11208132	3
Caelo	Citric acid monohydrate	1215911	1
Caelo	Citric acid monohydrate	1215907	1
Caelo	Citric acid monohydrate	12125907	6
Caelo	Citric acid monohydrate	12125938	1
Caelo	Citric acid monohydrate	12125904	2
Caelo	Citric acid monohydrate	13069110	4
Caelo	Citric acid monohydrate	13069128	3
Caelo	Citric acid monohydrate	14038401	6
Caelo	Citric acid monohydrate	13069129	4
Caelo	Citric acid monohydrate	13069133	5
Caelo	Citric acid monohydrate	14038403	8
Caelo	Citric acid monohydrate	14311808	4
Caelo	Citric acid monohydrate	14311812	4
Caelo	Citric acid monohydrate	15087509	8
Caelo	Citric acid monohydrate	15087510	2
Caelo	Citric acid monohydrate	15185314	4
Caelo	Citric acid monohydrate	15185321	3
Caelo	Citric acid monohydrate	15185320	3
Caelo	Citric acid monohydrate	16186501	2
Caelo	Citric acid monohydrate	14071701	1
Caelo	Citric acid monohydrate	17085603	5

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Supplier	Substance	Batch	Spectra
Caelo	Citric acid monohydrate	17329807	1
Caelo	Citric acid monohydrate	14311807	2
Caelo	Citric acid monohydrate	15087512	1
Caelo	Citric acid monohydrate	15185317	1
Caelo	Citric acid monohydrate	13069130	1
Caelo	Citric acid monohydrate	13069105	2
Caelo	Citric acid monohydrate	13069124	4
Caelo	Citric acid monohydrate	15087503	2
Caelo	Citric acid monohydrate	15185304	10
Caelo	Citric acid monohydrate	12125937	3
Caelo	Citric acid monohydrate	14311813	1
Caelo	Citric acid monohydrate	13069111	3
Caelo	Citric acid monohydrate	13069103	1
Caelo	Citric acid monohydrate	2515Q-02959	1
Caelo	Citric acid monohydrate	17085607	4
Caelo	Citric acid monohydrate	16186502	5
Caelo	Citric acid monohydrate	13069106	3
Caelo	Citric acid monohydrate	sjdfksjfdkl	1
Caelo	Citric acid monohydrate	161865001	1
Caelo	Citric acid monohydrate	17329808	1
Caelo	Citric acid monohydrate	18130503	2
Caelo	Citric acid monohydrate	19088402	1
Caelo	Citric acid monohydrate	19088401	2
Caelo	Citric acid monohydrate	15185302	12
Caelo	Citric acid monohydrate	15185316	5
Caelo	Citric acid monohydrate	17329804	6
Caelo	Citric acid monohydrate	18130510	1
Caelo	Citric acid monohydrate	17329801	1
Caesar & Loretz GmbH	Citric acid monohydrate	18130506	1
Caesar & Loretz GmbH	Citric acid monohydrate	12125937	1
Cealo	Citric acid monohydrate	15185320	1
E Plus	Citric acid monohydrate	16186508	1
Ebert 17.08.16	Citric acid monohydrate	15185314	1
Euro OTC	Citric acid monohydrate	17085607	1
Eurompharm / Gehe	Citric acid monohydrate	17329804	1
Fiebig28.08.13 EK6,60	Citric acid monohydrate	13069111	1
Hedinger / Phönix	Citric acid monohydrate	202029	1
Hedinger/Phönix	Citric acid monohydrate	202029	1
Caelo	Citric acid monohydrate	13069113	2
Caelo	Citric acid monohydrate	13069125	2
Krieger	Citric acid monohydrate	613001-1-P	1
Caelo	Citric acid monohydrate	15087502	2
Caelo	Citric acid monohydrate	15185309	2
Caelo	Citric acid monohydrate	16186508	5
Phönix	Citric acid monohydrate	10111503	1
Phönix	Citric acid monohydrate	1403/3	1
Sanacaorp	Citric acid monohydrate	14038401	2
Sanacorp	Citric acid monohydrate	1215937	1
Caelo	Citric acid monohydrate	11208133	4
VDL	Citric acid monohydrate	263669	1
Caelo	Citric acid monohydrate	15185301	2
Caelo	Citric acid monohydrate	17085602	8
Hedinger	Citric acid monohydrate	202029	2

- 111 028 spectra from 742 *Apo-Ident* customers from a total of 31 821 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Citric acid monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Citric acid monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	80	0	119 062
Type C	0	209	10	111 028

The substance/substance group *Citric acid monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	95.4338 % (> 94.0639 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Citric acid monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	34.54	—
Oxytetracycline hydrochloride	36.62	—
Doxycycline hyclate	49.24	—
Sodium tetraborate	49.61	—
Vancomycin hydrochloride	50.35	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Citric acid monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20926	23458	3.53	34.11
22340	23458	7.20	31.22
23409	23458	2.77	34.37
23457	23458	3.58	32.47
23458	23458	0.00	34.75
24874	23458	6.35	30.83
24222	24222	0.00	39.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Citrulline**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21095-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Citrulline; Citrullinum; L-citrulline

Special notes

When selecting the *Citrulline* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Citrulline	8	7	6

Second-stage model

For differentiation of the substance/substance group *Citrulline* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Citrulline*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Citrulline	1310015-01	21095	40	20131120
Euro OTC	Citrulline	1403021-01	21565	59	1411031
Euro OTC	Citrulline	1506014	21828	60	20150624*
Euro OTC	Citrulline	1604038	22560	40	20160523*
Euro OTC	Citrulline	1703036	23175	40	20170418*
Euro OTC	Citrulline	1811028	24348	40	20181127*
Fagron	Citrulline	16D11-B02-326797	23567	40	20160421
Fagron	Citrulline	18K15-B01-356962	24643	40	20190123

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 359 spectra of 8 reference samples from the substance/substance group *Citrulline*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 330 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Citrulline*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Citrulline	1609013	22866	40
Euro OTC	Citrulline	1707003	23538	40
Euro OTC	Citrulline	1710039	23913	40
Euro OTC	Citrulline	1805028	24117	40
Euro OTC	Citrulline	1904013	24627	40
Euro OTC	Citrulline	2001002	25070	40
Fagron	Citrulline	19E03-B01-362002	24819	40

- 118 862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 3 *Apo-Ident* customers from 7 batches from the substance/substance group *Citrulline*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Citrulline	17C14-B01-339452	2
Euro OTC	Citrulline	16040038-01	1
Fagron	Citrulline	18B12-B02	1
Fagron	Citrulline	18K15-B01	1
Gall-Pharma GmbH	Citrulline		1
Gall-Pharma GmbH/Noweda	Citrulline		1
Hecht-Pharma/ Noweda	Citrulline		1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Citrulline* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Citrulline* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	359	0	110 330
Type B	0	280	0	118 862
Type C	0	7	1	111 239

The substance/substance group *Citrulline* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3287 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Citrulline* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Colistin sulfate	30.67	—
Thiamine chloride hydrochloride	31.19	—
Bacitracin	34.79	—
Magnesium citrate	35.69	—
Polymyxin B sulfate	37.57	—
Nystatin	42.84	—
Clindamycin hydrochloride	49.69	—
Menthol	50.73	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Citrulline* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24643	21828	1.87	36.47
22560	22560	0.00	37.30

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21095	21565	7.17	34.79
21565	21565	0.00	35.03
24348	24348	0.00	33.82
23175	23175	0.00	37.90
21828	21828	0.00	36.02
23567	22560	3.09	37.44

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Clindamycin hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20214-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Clindamycin hydrochloride; Clindamycini hydrochloridum

Special notes

When selecting the *Clindamycin hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Clindamycin hydrochloride	8	6	157

Second-stage model

For differentiation of the substance/substance group *Clindamycin hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Clindamycin hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Clindamycin hydr...	15392809	22958	40	20151204
Caelo	Clindamycin hydr...	15392817	23245	40	20151204
Euro OTC	Clindamycin hydr...	1111058-01	20757	80	20120516
Euro OTC	Clindamycin hydr...	1511004	21996	60	20151123*
Euro OTC	Clindamycin hydr...	1510038	22224	60	20151120*
Euro OTC	Clindamycin hydr...	2001044	25074	40	20200303*
Fagron	Clindamycin hydr...	13G24-N09	21224	40	1412075
Fagron	Clindamycin hydr...	16D05-B08-332106	23264	40	20160504

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 8 reference samples from the substance/substance group *Clindamycin hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 289 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Clindamycin hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Clindamycin hydrochloride	153928	23365	40
Caelo	Clindamycin hydrochloride	172093	23681	40
Euro OTC	Clindamycin hydrochloride	1401041-01	21239	40
Euro OTC	Clindamycin hydrochloride	1710013	23769	40
Euro OTC	Clindamycin hydrochloride	1811003	24336	40
Euro OTC	Clindamycin hydrochloride	1903009	24637	40

- 118902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 368 spectra from 148 *Apo-Ident* customers from 165 batches from the substance/substance group *Clindamycin hydrochloride*.
- Among them are spectra of independent samples from 157 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Clindamycin hydrochloride	130402X5	1
AHD	Clindamycin hydrochloride	1710013-01	1
Caelo	Clindamycin hydrochloride	16H03-B03-334345	1
Fagron	Clindamycin hydrochloride	18A18-B08-346107	1
Anzag	Clindamycin hydrochloride	15392815	1
Bombastus	Clindamycin hydrochloride	1710013-01	1
Caelo	Clindamycin hydrochloride	17001301	1
Caelo	Clindamycin hydrochloride	1811003-01	2
Caelo	Clindamycin hydrochloride	11K04-N12	1
Caelo	Clindamycin hydrochloride	1111058-03	1
Caelo	Clindamycin hydrochloride	15392802	1
Caelo	Clindamycin hydrochloride	15L22-B03-318788	1
Caelo	Clindamycin hydrochloride	15392805	1
Caelo	Clindamycin hydrochloride	15189512	1
Caelo	Clindamycin hydrochloride	15392816	1
Caelo	Clindamycin hydrochloride	15392818	2
Caelo	Clindamycin hydrochloride	15392822	2
Caelo	Clindamycin hydrochloride	17209301	1
Caelo	Clindamycin hydrochloride	18A18-B08-346106	2
Caelo	Clindamycin hydrochloride	17209302	2
Caelo	Clindamycin hydrochloride	18009401	1
Caelo	Clindamycin hydrochloride	18009403	2
Caelo	Clindamycin hydrochloride	18009405	2
Caelo	Clindamycin hydrochloride	18J15-B04-355581	1
Caelo	Clindamycin hydrochloride	18009412	1
Caelo	Clindamycin hydrochloride	19139202	2
Caelo	Clindamycin hydrochloride	1511004-02	1

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Supplier	Substance	Batch	Spectra
Caelo	Clindamycin hydrochloride	18009413	1
Caelo	Clindamycin hydrochloride	1511004-03	2
Caelo	Clindamycin hydrochloride	1511004-01	3
Caelo	Clindamycin hydrochloride	3304	1
Caelo	Clindamycin hydrochloride	18009408	1
Caelo	Clindamycin hydrochloride	13G24-N09	1
Caelo	Clindamycin hydrochloride	19139203	2
Caelo	Clindamycin hydrochloride	151003801	2
Caelo	Clindamycin hydrochloride	15392811	2
Caelo	Clindamycin hydrochloride	15392819	1
Caelo	Clindamycin hydrochloride	18009409	1
Caelo	Clindamycin hydrochloride	P-003-WS10100301	1
Caelo	Clindamycin hydrochloride	1401041-01	2
Caelo	Clindamycin hydrochloride	15E06-B12-310472	1
Caelo	Clindamycin hydrochloride	15392807	1
Caelo	Clindamycin hydrochloride	15392815	3
Caelo	Clindamycin hydrochloride	15392814	1
Caelo	Clindamycin hydrochloride	17209303	2
Caelo	Clindamycin hydrochloride	160712C	2
Caelo	Clindamycin hydrochloride	10809406	1
Caelo	Clindamycin hydrochloride	18009406	1
Caelo	Clindamycin hydrochloride	15392804	3
Caelo	Clindamycin hydrochloride	16H03-B02	1
Caelo	Clindamycin hydrochloride	14K04B05309851	1
Caesar & Loretz GmbH	Clindamycin hydrochloride	19139202	1
Cealo	Clindamycin hydrochloride	1111058-01	1
Cealo/AHD	Clindamycin hydrochloride	16D05-B08-325088	1
Euro OTC	Clindamycin hydrochloride	1511004-02	4
EuRho	Clindamycin hydrochloride	1401041-01	1
EuRho	Clindamycin hydrochloride	1710013-01	1
Euro OTC	Clindamycin hydrochloride	140104102	3
Euro OTC	Clindamycin hydrochloride	700168	1
Euro OTC	Clindamycin hydrochloride	1510038-02	3
Euro OTC	Clindamycin hydrochloride	150901B	1
Euro OTC	Clindamycin hydrochloride	130709X8	2
Euro OTC	Clindamycin hydrochloride	25071401	1
Euro OTC	Clindamycin hydrochloride	140104101	1
Euro OTC	Clindamycin hydrochloride	1401401-01	1
Euro OTC	Clindamycin hydrochloride	151100401	2
Euro OTC	Clindamycin hydrochloride	8061801	1
Euro OTC	Clindamycin hydrochloride	171001301	1
Euro OTC	Clindamycin hydrochloride	111158-01	1
Euro OTC	Clindamycin hydrochloride	1111058-03	3
Euro OTC	Clindamycin hydrochloride	1401041-01	11
Euro OTC	Clindamycin hydrochloride	1401041-02	6
Euro OTC	Clindamycin hydrochloride	1511004-01	14
Euro OTC	Clindamycin hydrochloride	4988149	1
Euro OTC	Clindamycin hydrochloride	T03-05/1401041-01	1
Euro OTC	Clindamycin hydrochloride	2908019-01	1
Euro OTC	Clindamycin hydrochloride	2908019V-03	4
Euro OTC	Clindamycin hydrochloride	16H03-B02-334974	1
Euro OTC	Clindamycin hydrochloride	813M-03534	1
Euro OTC	Clindamycin hydrochloride	1511004-03	1
Euro OTC	Clindamycin hydrochloride	16H03-B02-339275	1
Euro OTC	Clindamycin hydrochloride	16D05-B08-328259	1
Euro/Gehe16.03.16	Clindamycin hydrochloride	1510038-01	1
Euro OTC	Clindamycin hydrochloride	SCHE1107035	1
Euro OTC	Clindamycin hydrochloride	1510030-01	1
Euro OTC	Clindamycin hydrochloride	1710013-01	16
Euro OTC	Clindamycin hydrochloride	1111058-02	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Clindamycin hydrochloride	1511004-002	1
Euro OTC	Clindamycin hydrochloride	1811003-01	5
Europharm/Otto	Clindamycin hydrochloride	1111058-01	1
Fagron	Clindamycin hydrochloride	15E06-B12-310472	1
Fagron	Clindamycin hydrochloride	16D05-B08-321572	1
Fagron	Clindamycin hydrochloride	16D05-B08-323321	1
Fagron	Clindamycin hydrochloride	16H03-B02-334344	1
Fagron	Clindamycin hydrochloride	12F19-N07	3
Fagron	Clindamycin hydrochloride	12C19-N06	1
Fagron	Clindamycin hydrochloride	13A22-N01	6
Fagron	Clindamycin hydrochloride	P003-WS10100301	1
Fagron	Clindamycin hydrochloride	13C15-N06	1
Fagron	Clindamycin hydrochloride	13G24N09	1
Fagron	Clindamycin hydrochloride	P003WS13091401	1
Fagron	Clindamycin hydrochloride	13J03-B02_288654	1
Fagron	Clindamycin hydrochloride	111105803	1
Fagron	Clindamycin hydrochloride	14D23-B03	1
Fagron	Clindamycin hydrochloride	14K04-B05-304996	1
Fagron	Clindamycin hydrochloride	15E06-B12-311886	4
Fagron	Clindamycin hydrochloride	14K04-B05-313090	1
Fagron	Clindamycin hydrochloride	15E06-B12-314066	1
Fagron	Clindamycin hydrochloride	P-003-CN20150406	1
Fagron	Clindamycin hydrochloride	15E06-B12-314064	1
Fagron	Clindamycin hydrochloride	15L22-B03-316670	1
Fagron	Clindamycin hydrochloride	2816	1
Fagron	Clindamycin hydrochloride	15L22-B03-318787	2
Fagron	Clindamycin hydrochloride	15E06-B12-314065	2
Fagron	Clindamycin hydrochloride	1600324C	1
Fagron	Clindamycin hydrochloride	16D05-B08-325088	3
Fagron	Clindamycin hydrochloride	16D05-B08-328259	1
Fagron	Clindamycin hydrochloride	16D05-B08-330624	1
Fagron	Clindamycin hydrochloride	16D05-B08-328260	1
Fagron	Clindamycin hydrochloride	16D05-B08-332107	1
Fagron	Clindamycin hydrochloride	16d05-b08-332107	1
Fagron	Clindamycin hydrochloride	16d05-b08-325089	1
Fagron	Clindamycin hydrochloride	16H03-B02-334345	1
Fagron	Clindamycin hydrochloride	16H03-B02-336706	5
Fagron	Clindamycin hydrochloride	18041801	1
Fagron	Clindamycin hydrochloride	160324C	1
Fagron	Clindamycin hydrochloride	16H03-B02	1
Fagron	Clindamycin hydrochloride	18D11-B01	3
Fagron	Clindamycin hydrochloride	K-171217B	2
Fagron	Clindamycin hydrochloride	18D11-B01-351175	1
Fagron	Clindamycin hydrochloride	K-180507B	1
Fagron	Clindamycin hydrochloride	16H03-B02-341602	2
Fagron	Clindamycin hydrochloride	18D11-B01-349677	2
Fagron	Clindamycin hydrochloride	18D11-B01-351176	1
Fagron	Clindamycin hydrochloride	18D11-B01-352733	2
Fagron	Clindamycin hydrochloride	13J03B02288654	1
Fagron	Clindamycin hydrochloride	16H03-B02-338802	2
Fagron	Clindamycin hydrochloride	18A18-B08	3
Fagron	Clindamycin hydrochloride	18D11-B01-352131	1
Fagron	Clindamycin hydrochloride	13A22/N01	1
Fagron	Clindamycin hydrochloride	16D05-B08-320327	3
Fagron	Clindamycin hydrochloride	16D05-B08-332105	1
Fagron	Clindamycin hydrochloride	18A18-B08-347483	3
Fagron	Clindamycin hydrochloride	13J03-B02-288654	3
Fagron	Clindamycin hydrochloride	16H03-B02-334974	1
Fagron	Clindamycin hydrochloride	16-H03-B02-341602	1
Fagron	Clindamycin hydrochloride	18J15-B04-355579	1

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Supplier	Substance	Batch	Spectra
Fagron	Clindamycin hydrochloride	18J15-B04-360142	1
Fagron	Clindamycin hydrochloride	16D05-B08	2
Fagron	Clindamycin hydrochloride	16D05-B08-327127	5
Fagron	Clindamycin hydrochloride	18D11-B01-351866	1
Fagron	Clindamycin hydrochloride	13j03-B02-288653	1
Fagron	Clindamycin hydrochloride	16D05-B08-325087	1
Fagron	Clindamycin hydrochloride	13J03-B02-288655	1
Fagron	Clindamycin hydrochloride	2714Q-03534	1
Fagron	Clindamycin hydrochloride	1010616	1
Fagron	Clindamycin hydrochloride	16H03-B02-341602	1
Fagron	Clindamycin hydrochloride	18J15-B04	1
Fagron	Clindamycin hydrochloride	18D11B01	1
Fagron	Clindamycin hydrochloride	14K04-B05-304995	1
Fagron	Clindamycin hydrochloride	14K04-B05-309851	1
Fagron	Clindamycin hydrochloride	18j15-b04-360142	1
Fagron	Clindamycin hydrochloride	19H28-F06-364301	1
Fagron	Clindamycin hydrochloride	13J03-B02	1
Fagron	Clindamycin hydrochloride	16H03-B02-338803	2
Fagron	Clindamycin hydrochloride	16H03-B02-339275	1
Fagron	Clindamycin hydrochloride	18D11-B01-353162	1
Fagron	Clindamycin hydrochloride	K-190507B	1
Fargon	Clindamycin hydrochloride	11L20-No5	1
Fargon	Clindamycin hydrochloride	16D05-B08-320327	1
Gehe	Clindamycin hydrochloride	11E12-N02	1
Gehe	Clindamycin hydrochloride	11K04-N12	1
Gehe	Clindamycin hydrochloride	700168-0002	1
Gehe	Clindamycin hydrochloride	13a22-n01	1
Gehe	Clindamycin hydrochloride	13A22-N01	1
GEHE	Clindamycin hydrochloride	1811003-01	1
Caelo	Clindamycin hydrochloride	140104102	1
Jenne	Clindamycin hydrochloride	18D11-B01-352732	2
Jenne	Clindamycin hydrochloride	18J15-B04-360142	1
L12	Clindamycin hydrochloride	18009403	2
L12	Clindamycin hydrochloride	17209302	1
L12	Clindamycin hydrochloride	18009402	2
L30	Clindamycin hydrochloride	17209301	1
noweda	Clindamycin hydrochloride	1511004-03	1
Noweda	Clindamycin hydrochloride	2908019V-03	1
Fagron	Clindamycin hydrochloride	18A18-B08-346106	1
Euro OTC	Clindamycin hydrochloride	1510038-01	18
Phoenix	Clindamycin hydrochloride	16D05-B08-327127	1
Phoenix	Clindamycin hydrochloride	1710013-010	1
Phoenix	Clindamycin hydrochloride	1811003-01	1
Phoenix	Clindamycin hydrochloride	3367	1
Phoenix 5.12.2018	Clindamycin hydrochloride	18A18-B08-346106	1
phönix	Clindamycin hydrochloride	15392820	1
Phönix	Clindamycin hydrochloride	12H30-N04	1
Phönix	Clindamycin hydrochloride	15392803	1
Sanacorp	Clindamycin hydrochloride	1511004-03	1
Sanacorp	Clindamycin hydrochloride	16D05-B08-332106	1
Sanacorp	Clindamycin hydrochloride	16H03-B02-341602	1
Sanacorp	Clindamycin hydrochloride	16H03-B02-339275	1
Sanacorp	Clindamycin hydrochloride	18A18-B08-347483	1
Sanacorp	Clindamycin hydrochloride	K-171219B	1
Sanacorp	Clindamycin hydrochloride	18D11-B01-352732	1
Fagron	Clindamycin hydrochloride	15E06-B12-313089	2
Spangro 22.05.2014	Clindamycin hydrochloride	13G24-N09	1
Spangro_04.04.2019	Clindamycin hydrochloride	18D11-B01-352131	1
Caelo	Clindamycin hydrochloride		1
Caelo	Clindamycin hydrochloride	15392817	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Clindamycin hydrochloride	1111058-01	6
Fagron	Clindamycin hydrochloride	13G24-N09	7
Fagron	Clindamycin hydrochloride	16D05-B08-332106	4

- 110 879 spectra from 742 *Apo-Ident* customers from a total of 31 729 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clindamycin hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clindamycin hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	240	0	118 902
Type C	0	362	6	110 879

The substance/substance group *Clindamycin hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	98.3696 % (> 97.5543 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Clindamycin hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Polymyxin B sulfate	22.74	—
Bacitracin	28.16	—
Colistin sulfate	31.78	—

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Substanz	Distance in main model	Distance in second-stage model
Magnesium citrate	36.74	—
Minoxidil	41.98	—
Cyanocobalamin	45.08	—
Prednisone	48.02	—
Riboflavin	48.87	—
Citrulline	53.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Clindamycin hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20757	21996	1.96	25.46
21224	21224	0.00	21.24
21996	21996	0.00	23.44
22224	22224	0.00	21.88
22958	21996	3.28	23.72
23245	21996	3.34	23.02
23264	21996	2.33	23.22
25074	25074	0.00	30.87

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Clioquinol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20095-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Clioquinol; Clioquinolum

Special notes

When selecting the *Clioquinol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Clioquinol	6	7	221

Second-stage model

For differentiation of the substance/substance group *Clioquinol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Clioquinol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Clioquinol	11304120	20895	40	20111208
Caelo	Clioquinol	163072	23047	40	20161202*
Euro OTC	Clioquinol	1309009-02	21246	40	AR-15-FG-009542-01
Euro OTC	Clioquinol	1509038	21944	60	20151009*
Fagron	Clioquinol	13I26-N15	21236	40	20131028
Fagron	Clioquinol	14I11-B03-300049	21913	60	20140926
Fagron	Clioquinol	14I11-B03-300049	21972	60	20140926

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Clioquinol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 349 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Clioquinol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Clioquinol	13114413	21308	40
Caelo	Clioquinol	16307206	22960	40
Caelo	Clioquinol	172046	23633	40
Caelo	Clioquinol	182782	24374	40
Euro OTC	Clioquinol	1612020	22985	40
Euro OTC	Clioquinol	1903010	24624	40
Euro OTC	Clioquinol	1910030	24968	40

- 118862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 924 spectra from 391 *Apo-Ident* customers from 231 batches from the substance/substance group *Clioquinol*.
- Among them are spectra of independent samples from 220 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Clioquinol	18B05-B07-345483	2
AHD	Clioquinol	18011502	1
Caelo	Clioquinol	1509038-01	1
Euro OTC	Clioquinol	16307216	1
anzag	Clioquinol	13114418	1
Anzag	Clioquinol	12L04-N08	1
Caelo	Clioquinol	14359118	10
Apo-ident	Clioquinol	1509038-02	1
Axyntis Group	Clioquinol	1301014-02	1
Axyntis Group	Clioquinol	1301014-03	1
Bombastus	Clioquinol	1509038-03	1
Bombastus	Clioquinol	14359118	1
Cael Sanacorp 05.02.2016	Clioquinol	14359103	1
Caelo	Clioquinol	12F20-N05	1
Caelo	Clioquinol	3041409	1
Caelo	Clioquinol	10341605	4
Caelo	Clioquinol	10341601	2
Caelo	Clioquinol	1201034-01	1
Caelo	Clioquinol	11304103	2
Caelo	Clioquinol	11304111	2
Caelo	Clioquinol	11304112	6
Caelo	Clioquinol	5031302	1
Caelo	Clioquinol	10341608	1
Caelo	Clioquinol	11304105	3
Caelo	Clioquinol	11304116	3
Caelo	Clioquinol	11304117	10

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Supplier	Substance	Batch	Spectra
Caelo	Clioquinol	13114404	2
Caelo	Clioquinol	11304119	3
Caelo	Clioquinol	11304109	1
Caelo	Clioquinol	11304124	13
Caelo	Clioquinol	13114406	1
Caelo	Clioquinol	13114408	3
Caelo	Clioquinol	13114410	2
Caelo	Clioquinol	13114415	3
Caelo	Clioquinol	13114417	7
Caelo	Clioquinol	1309009-02	1
Caelo	Clioquinol	13114424	10
Caelo	Clioquinol	16021505	1
Caelo	Clioquinol	13114421	1
Caelo	Clioquinol	13114427	2
Caelo	Clioquinol	8714	1
Caelo	Clioquinol	2773	1
Caelo	Clioquinol	144359111	1
Caelo	Clioquinol	1509038-02	2
Caelo	Clioquinol	160916CL	1
Caelo	Clioquinol	16307204	1
Caelo	Clioquinol	16307207	18
Caelo	Clioquinol	1509038-03	3
Caelo	Clioquinol	16118-B04-329141	1
Caelo	Clioquinol	16307209	1
Caelo	Clioquinol	16307211	6
Caelo	Clioquinol	4111707	1
Caelo	Clioquinol	16307213	1
Caelo	Clioquinol	17204601	3
Caelo	Clioquinol	18121714	1
Caelo	Clioquinol	16307215	9
Caelo	Clioquinol	16122020-01	1
Caelo	Clioquinol	18011502	34
Caelo	Clioquinol	180115117	1
Caelo	Clioquinol	18278206	6
Caelo	Clioquinol	18278215	2
Caelo	Clioquinol	14359120	7
Caelo	Clioquinol	1201034-02	2
Caelo	Clioquinol	18011511	2
Caelo	Clioquinol	1130312	1
Caelo	Clioquinol	16307206	19
Caelo	Clioquinol	17204603	15
Caelo	Clioquinol	16307208	12
Caelo	Clioquinol	10341510	1
Caelo	Clioquinol	150903803	1
Caelo	Clioquinol	16307203	3
Caelo	Clioquinol	4214Q-02562	1
Caelo	Clioquinol	14359103	9
Caelo	Clioquinol	15L30-B05-314974	1
Caelo	Clioquinol	11 (18011523)	1
Caelo	Clioquinol	15L30-B05-321899	2
Caelo	Clioquinol	1509038-OTC-Pharma	1
Caelo	Clioquinol	14C21-B06-293104	1
Caelo	Clioquinol	14353120	1
Caelo	Clioquinol	1405080031	1
Caelo	Clioquinol	18278214	3
Caelo	Clioquinol	14359119	4
Caelo	Clioquinol	11304113	4
Caelo	Clioquinol	130114-02	1
Caelo	Clioquinol	14359117	4
Caelo	Clioquinol	14/11-B03-309181	1

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Supplier	Substance	Batch	Spectra
Caelo	Clioquinol	182782002	1
Caelo	Clioquinol	14359116	1
Caelo	Clioquinol	18011523	8
Caelo	Clioquinol	11304102	7
Caelo	Clioquinol	13A29-N07	1
Caelo	Clioquinol	3513I-02562	1
Caelo	Clioquinol	13114413	10
Caelo	Clioquinol	13114422	7
Caelo	Clioquinol	14359112	14
Caelo	Clioquinol	16307210	4
Caelo	Clioquinol	18E08-B06-355575	2
Caelo	Clioquinol	4613E2562	1
Caelo	Clioquinol	1405080036	1
Caelo	Clioquinol	18011501	2
Caelo	Clioquinol	18011527	1
Caelo	Clioquinol	5089	1
Caelo	Clioquinol	170926CL/16307208	1
Caelo	Clioquinol	16J18-B04-328520	1
Caelo	Clioquinol	180127C/16307215	1
Caelo	Clioquinol	3713A2562	1
Caelo	Clioquinol	1214I02562	1
Caelo	Clioquinol	13114418	5
Caelo	Clioquinol	1612020-01	2
Caelo	Clioquinol	14359102	11
Caelo	Clioquinol	12L04-N08	2
Caelo	Clioquinol	5213A2562	1
Caelo	Clioquinol	14/-B03-309181	1
Caelo	Clioquinol	14/11-BG03-309181	1
Caelo	Clioquinol	16307216	11
Caelo	Clioquinol	11304107	5
Caelo	Clioquinol	13114423	10
Caelo	Clioquinol	16307205	10
Caelo	Clioquinol	103415	2
Caelo	Clioquinol	1612020-02	1
Caelo	Clioquinol	14359111	13
Caesar & Loretz GmbH	Clioquinol	16307207	1
Caesar & Loretz GmbH	Clioquinol	16307216	1
Caesar & Loretz GmbH	Clioquinol	18011516	2
Caesar & Loretz GmbH	Clioquinol	18011517	1
Caesar & Loretz GmbH	Clioquinol	18011523	1
Caesar & Loretz GmbH	Clioquinol	18278214	1
Caesar & Loretz GmbH/Alli	Clioquinol	18278215	1
Caesar & Loretz GmbH/Fi...	Clioquinol	18011502	1
Caesar & Loretz GmbH/Kr...	Clioquinol	18278202	1
caesar&lorenz,Phönix	Clioquinol	14359111	1
Caolo- Noweda	Clioquinol	14359118	1
Cealo/Sanacorp	Clioquinol	1309009-01	1
EuRho	Clioquinol	1201034-02	1
EuRho	Clioquinol	1309009-02	1
EuRho	Clioquinol	1612020-01	1
EuRho	Clioquinol	161202001	1
Euro	Clioquinol	1509038-01	2
EURO / Sanacorp	Clioquinol	150903802	1
Euro OTC	Clioquinol	130900902	1
Euro OTC	Clioquinol	150903802	2
Euro OTC	Clioquinol	14359118	1
Euro OTC	Clioquinol	16307208	1
Euro OTC	Clioquinol	1612020	1
Euro OTC	Clioquinol	1612020-03	1
Euro OTC	Clioquinol	1509038-0	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Clioquinol	1309009-01	6
Euro OTC	Clioquinol	1409031-02	10
Euro OTC	Clioquinol	1409031-01	5
Euro OTC	Clioquinol	1201034-01	5
Euro OTC	Clioquinol	1301014-02	5
Euro OTC	Clioquinol	13010104-03	1
Euro OTC	Clioquinol	1305070109	1
Euro OTC	Clioquinol	140903101	1
Euro OTC	Clioquinol	14359120	1
Euro OTC	Clioquinol	120103402	1
Euro OTC	Clioquinol	1102022-02	3
Euro OTC	Clioquinol	1201034-02	8
Euro OTC	Clioquinol	1301014	1
Euro OTC	Clioquinol	2195137	1
Euro OTC	Clioquinol	1301014-01	2
Euro OTC	Clioquinol	PC86	1
Euro OTC	Clioquinol	1509038-01	10
Euro OTC	Clioquinol	1102022-01	2
Euro OTC	Clioquinol	14090131-02	1
Euro OTC	Clioquinol	1509038-31	1
Euro OTC	Clioquinol	161202001	2
Euro OTC	Clioquinol	1612020-02	3
Euro OTC	Clioquinol	1303009-02	1
Euro OTC	Clioquinol	1612020-01	27
Euro OTC	Clioquinol	1509038-04	3
Euro OTC	Clioquinol	1612020_01	2
Euro/Phoenix	Clioquinol	1612020-02	3
Euro/Phönix	Clioquinol	1509038-02	1
Euro OTC	Clioquinol	150903-01	1
Euro OTC	Clioquinol	1509038-02	29
Euro OTC	Clioquinol	1213A-02562	1
Fagron	Clioquinol	13F12-N20	2
Fagron	Clioquinol	11G20-N09	1
Fagron	Clioquinol	1005090024	1
Fagron	Clioquinol	12F20-N05	3
Fagron	Clioquinol	13A29-N07	7
Fagron	Clioquinol	13D15-N01	8
Fagron	Clioquinol	13DS15-N01	1
Fagron	Clioquinol	28031401	1
Fagron	Clioquinol	13I26N15	1
Fagron	Clioquinol	14052014C	1
Fagron	Clioquinol	1326-N15	3
Fagron	Clioquinol	13114417	1
Fagron	Clioquinol	14C21-B06-293104	6
Fagron	Clioquinol	14-C21-B06-293132	1
Fagron	Clioquinol	14C21-B06-293132	2
Fagron	Clioquinol	14C21-B08	1
Fagron	Clioquinol	14C21-B06	2
Fagron	Clioquinol	1309009-01	1
Fagron	Clioquinol	14/11-B03-300049	3
Fagron	Clioquinol	1411-B03-300049	3
Fagron	Clioquinol	1411B03300049	1
Fagron	Clioquinol	14/11-803-309181	1
Fagron	Clioquinol	14359118	1
Fagron	Clioquinol	1505120044	1
Fagron	Clioquinol	15L30-B05	2
Fagron	Clioquinol	14111-B03-300049	1
Fagron	Clioquinol	15L30-B05-321899	6
Fagron	Clioquinol	16J18-B04-328520	2
Fagron	Clioquinol	15L30-321899	1

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Supplier	Substance	Batch	Spectra
Fagron	Clioquinol	15L30-B05-321899	1
Fagron	Clioquinol	14/11-Bo3	1
Fagron	Clioquinol	16J18-B04	2
Fagron	Clioquinol	16J18-B04-32914	1
Fagron	Clioquinol	1618B04-329141	1
Fagron	Clioquinol	16J18-B04-332852	4
Fagron	Clioquinol	18B05-B07-347586	3
Fagron	Clioquinol	18805-B07-3475B6	1
Fagron	Clioquinol	18E08-B06-355575	1
Fagron	Clioquinol	1411-B03-309181	1
Fagron	Clioquinol	16/18-b04-328511	1
Fagron	Clioquinol	16J18-B04-328511	5
Fagron	Clioquinol	11K21-N18	4
Fagron	Clioquinol	16/18-B04-328511	1
Fagron	Clioquinol	11G20/N09	1
Fagron	Clioquinol	13/26-N15	2
Fagron	Clioquinol	13F12-N200463480	1
Fagron	Clioquinol	18B05-B07	2
Fagron	Clioquinol	11304112	1
Fagron	Clioquinol	14C21B06293104	1
Fagron	Clioquinol	16J18-B04-329704	1
Fagron	Clioquinol	16J18-B04-332861	1
Fagron	Clioquinol	14C21-B06-297159	3
Fagron	Clioquinol	19F17-B07-191239	2
Fagron	Clioquinol	16J18-B04-329141	4
Fagron	Clioquinol	14I11-B03	2
Fagron	Clioquinol	14I11-B03-309048	2
Fagron	Clioquinol	14I11-B03-309181	2
Fagron	Clioquinol	15L30-B05-314974	8
Fagron	Clioquinol	1605100008	1
Fagron	Clioquinol	16/18-B04-332852	1
Fagron	Clioquinol	18E08-B06-352127	1
Fagron	Clioquinol	15L30-B05-319616	2
Fagron	Clioquinol	1305120028	1
Fagron	Clioquinol	14I11-B03-3000049	1
Fagron	Clioquinol	3916U-02562	1
Fagron	Clioquinol	18E08-B06355575	1
Fagron	Clioquinol	18E08-B06	3
Fagron	Clioquinol	14/11-B03-309181	3
Fagron	Clioquinol	7D20-N03	1
Fagron	Clioquinol	11304120	1
Fagron	Clioquinol	2014Q2562	1
Fagron	Clioquinol	2514U2562	1
Fagron	Clioquinol	14I11B03300049	1
Fagron	Clioquinol	14C21806293104	1
Fagron	Clioquinol	1205110014	1
Fagron	Clioquinol	14c21B06293104	1
Fagron	Clioquinol	1411-813	1
Fagron	Clioquinol	16J18B04	1
Fagron	Clioquinol	13A29-N07-3398310111	1
Fiebig	Clioquinol	1409031-02	2
Fiebig	Clioquinol	14/11-B03-300048	1
Gatt-Koller	Clioquinol	1802295	2
Gehe	Clioquinol	1509038-03	1
GEHE	Clioquinol	1509038-03	1
GEHE	Clioquinol	1509038-02	1
GEHE	Clioquinol	18B05-B07	1
GEHE 04.08.2014	Clioquinol	13114418	1
Klenk	Clioquinol	11304120	1
L12	Clioquinol	1509038-03	2

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Supplier	Substance	Batch	Spectra
L12	Clioquinol	1612020-01	2
Nachprüfung	Clioquinol	3021U-02562	1
Nachprüfung	Clioquinol	13L26-N15	2
Noweda	Clioquinol	11304111	1
Noweda	Clioquinol	1201034-02	2
Noweda	Clioquinol	11304107	1
Noweda	Clioquinol	10057206	1
Noweda	Clioquinol	1309009-01	1
Noweda	Clioquinol	14359103	1
Noweda	Clioquinol	14359120	1
Noweda	Clioquinol	16307208	1
Noweda	Clioquinol	18278214	1
Noweda	Clioquinol	1903010-01	1
Fagron	Clioquinol	12L04-N08	7
Fagron	Clioquinol	13114424	1
Euro OTC	Clioquinol	2507212562	1
Euro OTC	Clioquinol	1509038-03	19
Phoenix	Clioquinol	11304119	1
Phoenix	Clioquinol	13114408	2
Phoenix	Clioquinol	13114417	1
Phoenix	Clioquinol	16J18-B04-332852	2
Phoenix	Clioquinol	18011523	1
Phoenix	Clioquinol	1612020-02	1
Phoenix	Clioquinol	18278206	1
Phönix	Clioquinol	1201034-02	1
Phönix	Clioquinol	1102022-02	3
Phönix	Clioquinol	14C21-B08	1
Phönix	Clioquinol	13114417	1
Phönix	Clioquinol	1309009-02	1
Phönix	Clioquinol	14C21-B06	2
Phönix	Clioquinol	16718b04332852	1
Phönix	Clioquinol	3165	1
Phönix	Clioquinol	15L30-B05-314974	1
Caelo	Clioquinol	16307214	12
Phönix Gotha	Clioquinol	11304124	1
Caelo	Clioquinol	18011516	15
Sanacorp	Clioquinol	11304111	1
Sanacorp	Clioquinol	1201034-01	1
Sanacorp	Clioquinol	11304124	1
Sanacorp	Clioquinol	13114422	1
Sanacorp	Clioquinol	8/AKD4	1
Sanacorp	Clioquinol	16J18-B04-328511	1
Sanacorp04	Clioquinol	1612020-02	1
Synthexim	Clioquinol	1405080036	1
Caelo	Clioquinol	14359113	2
Unisan	Clioquinol	14/11-B03	1
VDL	Clioquinol	131144131	1
wepa/Sanaco	Clioquinol	1439118	1
Euro OTC	Clioquinol	1309009-02	14
Caelo	Clioquinol	11304120	12
Caelo	Clioquinol	163072	1
Euro OTC	Clioquinol	1509038	2
Euro OTC	Clioquinol		1
Fagron	Clioquinol	13I26-N15	4
Fagron	Clioquinol	14I11-B03-300049	6
Fagron	Clioquinol		1
phönix	Clioquinol		1

- 110 323 spectra from 742 *Apo-Ident* customers from a total of 31 662 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clioquinol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clioquinol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	280	0	118 862
Type C	0	792	132	110 323

The substance/substance group *Clioquinol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	85.7143 % (> 85.3896 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Clioquinol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sulfogaiacol hydrate	35.22	—
Midazolam hydrochloride	41.94	—
Miconazole nitrate	46.03	—
L-tryptophan	48.10	—
Acetylsalicylic acid	56.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Clioquinol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20895	21246	4.12	58.37
21236	21246	3.36	57.54
21246	21246	0.00	58.96
21913	21944	3.41	59.27
21944	21944	0.00	58.39
21972	21944	5.00	57.91
23047	23047	0.00	57.81

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Clobetasol propionate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20030-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Clobetasol propionate; Clobetasoli propionas

Special notes

When selecting the *Clobetasol propionate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Clobetasol propionate	8	6	356

Second-stage model

For differentiation of the substance/substance group *Clobetasol propionate* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Clobetasol propionate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Clobetasol propi...	13134705	21092	80	AR-15-FG-005328-01
Caelo	Clobetasol propi...	13269505	21473	60	AR-15-FG-000622-02
Caelo	Clobetasol propi...	14338001	21802	60	AR-16-FG-008581-01
Caelo	Clobetasol propi...	14338001	21802SI	59	AR-16-FG-008581-01
Caelo	Clobetasol propi...	14338001	21896	59	1607072
Caelo	Clobetasol propi...	14338001	21896SI	45	1607072
Caelo	Clobetasol propi...	15439504	22724	40	20160204
Caelo	Clobetasol propi...	15439504	22724SI	37	20160204
Caelo	Clobetasol propi...	192245	24904	40	20200127*
Euro OTC	Clobetasol propi...	1211021-04	21611	60	1605044
Euro OTC	Clobetasol propi...	1606022	22714	40	20160713*
Euro OTC	Clobetasol propi...	1606022	22714SI	40	20160713*
Fagron	Clobetasol propi...	18I12-B02-357669	24691	40	20181001

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 660 spectra of 13 reference samples from the substance/substance group *Clobetasol propionate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 029 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 530 spectra of 14 reference samples from the substance/substance group *Clobetasol propionate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Clobetasol propionate	161067	22470	60
Caelo	Clobetasol propionate	170967	23665	40
Euro OTC	Clobetasol propionate	1704020	23397	40
Euro OTC	Clobetasol propionate	1804002	24075	40
Euro OTC	Clobetasol propionate	1903014	24615	40
Fagron	Clobetasol propionate	19B06-B03-360421	24822	40
Caelo	Clobetasol propionate	161067	22470SI	48
Caelo	Clobetasol propionate	170967	23665SI	20
Caelo	Clobetasol propionate	192245	24904SI [†]	40
Euro OTC	Clobetasol propionate	1704020	23397SI	20
Euro OTC	Clobetasol propionate	1804002	24075SI	22
Euro OTC	Clobetasol propionate	1903014	24615SI	40
Fagron	Clobetasol propionate	18I12-B02-357669	24691SI [†]	40
Fagron	Clobetasol propionate	19B06-B03-360421	24822SI	40

- 118 612 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1926 spectra from 558 *Apo-Ident* customers from 374 batches from the substance/substance group *Clobetasol propionate*.
- Among them are spectra of independent samples from 356 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
/Sanacorp	Clobetasol propionate	1804002-01	3
170420-01	Clobetasol propionate	17A057	1
20.12.2016 Phoenix 17,49EUR	Clobetasol propionate	15439504	1
Caelo	Clobetasol propionate	2x17325602	1
Fagron	Clobetasol propionate	16E04-B12-321034	2
Euro OTC	Clobetasol propionate	1211021/02	1
AHZ	Clobetasol propionate	1606022	1
Euro OTC	Clobetasol propionate	1211021-03	29
Euro OTC	Clobetasol propionate	1408018-02	71
Alliance	Clobetasol propionate	12342305	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Alliance H.	Clobetasol propionate	15234002	2
Alliance Health 17.01.2...	Clobetasol propionate	APB00547/112010C	1
Alliance Healthcare	Clobetasol propionate	12J25-N01	1
Alliance Healthcare	Clobetasol propionate	18082714	1
Euro OTC	Clobetasol propionate	1211021-02	31
allianz	Clobetasol propionate	15234009	1
Allianz	Clobetasol propionate	17325606	1
Allianz Healthcare 02.0...	Clobetasol propionate	1408018-01	1
Anzag	Clobetasol propionate	12E08-N04	1
Anzag	Clobetasol propionate	1211021-02	1
Anzag	Clobetasol propionate	1408018-01	2
Anzag	Clobetasol propionate	15246001	1
Anzag	Clobetasol propionate	16106703	1
Fagron	Clobetasol propionate	NT0421M	3
Apomix	Clobetasol propionate	16G18-B02-325571	1
Apomix/Phönix	Clobetasol propionate	1211021-03	1
Audor Pharma	Clobetasol propionate	sieheBemerkung	1
Audor Pharma	Clobetasol propionate	APCL0102/0518C	2
Audor Pharma	Clobetasol propionate	APCLP/M/036/16C	2
Audor Pharma	Clobetasol propionate	APAPL/035/E-12C	2
Audor Pharma	Clobetasol propionate	APL035E12C	1
Audor Pharma	Clobetasol propionate	APB0054/112010C	1
Audor Pharma	Clobetasol propionate	APL/035/E-12C	1
Bombastus	Clobetasol propionate	13G23-N01	1
Bombastus	Clobetasol propionate	13G23-N0	1
Bombastus	Clobetasol propionate	12342303	1
Caelo	Clobetasol propionate	14g30bo7302114	1
Caelo	Clobetasol propionate	1616715	1
Caelo	Clobetasol propionate	18082702	3
Caelo	Clobetasol propionate	18082717	1
Caelo	Clobetasol propionate	11101315	1
Caelo	Clobetasol propionate	11300702	3
Caelo	Clobetasol propionate	12107607	6
Caelo	Clobetasol propionate	23111202	1
Caelo	Clobetasol propionate	12107606	1
Caelo	Clobetasol propionate	20121012-4	1
Caelo	Clobetasol propionate	12107604	1
Caelo	Clobetasol propionate	12107609	6
Caelo	Clobetasol propionate	3012Q02835	1
Caelo	Clobetasol propionate	12342303	1
Caelo	Clobetasol propionate	12342306	6
Caelo	Clobetasol propionate	1108044-02	1
Caelo	Clobetasol propionate	31071302	1
Caelo	Clobetasol propionate	13A02-N04	1
Caelo	Clobetasol propionate	13134703	4
Caelo	Clobetasol propionate	13134702	7
Caelo	Clobetasol propionate	12342312	1
Caelo	Clobetasol propionate	13134704	4
Caelo	Clobetasol propionate	15031401	1
Caelo	Clobetasol propionate	13269501	1
Caelo	Clobetasol propionate	13269504	6
Caelo	Clobetasol propionate	13269508	13
Caelo	Clobetasol propionate	13K08-B30-287726	1
Caelo	Clobetasol propionate	14188502	8
Caelo	Clobetasol propionate	14102416	1
Caelo	Clobetasol propionate	14188504	6
Caelo	Clobetasol propionate	14188501	3
Caelo	Clobetasol propionate	14C03-B07-293560	2
Caelo	Clobetasol propionate	14338002	1
Caelo	Clobetasol propionate	14188506	3

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Supplier	Substance	Batch	Spectra
Caelo	Clobetasol propionate	14338006	11
Caelo	Clobetasol propionate	15246001	6
Caelo	Clobetasol propionate	14G30_B07_302114	1
Caelo	Clobetasol propionate	15234004	22
Caelo	Clobetasol propionate	15234001	9
Caelo	Clobetasol propionate	2778	1
Caelo	Clobetasol propionate	123645	1
Caelo	Clobetasol propionate	2829	1
Caelo	Clobetasol propionate	15J-15-B04-316616	1
Caelo	Clobetasol propionate	160115CP	1
Caelo	Clobetasol propionate	160829CP	1
Caelo	Clobetasol propionate	16E04-B12-321036	1
Caelo	Clobetasol propionate	15j15-b04-317698	1
Caelo	Clobetasol propionate	1606022-01	3
Caelo	Clobetasol propionate	15253032	1
Caelo	Clobetasol propionate	15439507	2
Caelo	Clobetasol propionate	16E04-B12	1
Caelo	Clobetasol propionate	154390504	1
Caelo	Clobetasol propionate	16106704	21
Caelo	Clobetasol propionate	18H22-B017-328012	1
Caelo	Clobetasol propionate	16H22-B07-328012	1
Caelo	Clobetasol propionate	12E08-N04	1
Caelo	Clobetasol propionate	16106710	6
Caelo	Clobetasol propionate	16107704	1
Caelo	Clobetasol propionate	16106715	9
Caelo	Clobetasol propionate	16348001	1
Caelo	Clobetasol propionate	1606022-025349	1
Caelo	Clobetasol propionate	15412910	1
Caelo	Clobetasol propionate	1704020-01	14
Caelo	Clobetasol propionate	170402001	2
Caelo	Clobetasol propionate	17096707	8
Caelo	Clobetasol propionate	16106719	4
Caelo	Clobetasol propionate	17096709	8
Caelo	Clobetasol propionate	17325602	24
Caelo	Clobetasol propionate	17090708	1
Caelo	Clobetasol propionate	17325601	9
Caelo	Clobetasol propionate	1105044-03	1
Caelo	Clobetasol propionate	17G14-B12-341742	1
Caelo	Clobetasol propionate	18082708	14
Caelo	Clobetasol propionate	18/12-B02-35480	1
Caelo	Clobetasol propionate	18082711	2
Caelo	Clobetasol propionate	18082714	4
Caelo	Clobetasol propionate	16106713	6
Caelo	Clobetasol propionate	1616703	1
Caelo	Clobetasol propionate	18300208	9
Caelo	Clobetasol propionate	11300703	5
Caelo	Clobetasol propionate	12342307	3
Caelo	Clobetasol propionate	16106701	3
Caelo	Clobetasol propionate	16106718	2
Caelo	Clobetasol propionate	1369504	1
Caelo	Clobetasol propionate	18082703	15
Caelo	Clobetasol propionate	18082710	5
Caelo	Clobetasol propionate	15234008	1
Caelo	Clobetasol propionate	1606022-02	6
Caelo	Clobetasol propionate	13269507	3
Caelo	Clobetasol propionate	18082709	17
Caelo	Clobetasol propionate	12342308	1
Caelo	Clobetasol propionate	14G30-B07-302114	2
Caelo	Clobetasol propionate	1804002-01	2
Caelo	Clobetasol propionate	18/12-B02-353203	1

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Supplier	Substance	Batch	Spectra
Caelo	Clobetasol propionate	18300213	4
Caelo	Clobetasol propionate	1108044-03	2
Caelo	Clobetasol propionate	11300707	2
Caelo	Clobetasol propionate	15234009	6
Caelo	Clobetasol propionate	170404CP1606022-02	1
Caelo	Clobetasol propionate	1108044-04	1
Caelo	Clobetasol propionate	1408018-03	9
Caelo	Clobetasol propionate	15439502	8
Caelo	Clobetasol propionate	13269509	1
Caelo	Clobetasol propionate	17325603	16
Caelo	Clobetasol propionate	18300202	1
Caelo	Clobetasol propionate	181016709	1
Caelo	Clobetasol propionate	11101311	1
Caelo	Clobetasol propionate	18082718	5
Caelo	Clobetasol propionate	12107608	1
Caelo	Clobetasol propionate	12342309	13
Caelo	Clobetasol propionate	13134701	16
Caelo	Clobetasol propionate	13G23-N01	1
Caelo	Clobetasol propionate	13269502	3
Caelo	Clobetasol propionate	2014E-02835	1
Caelo	Clobetasol propionate	14338005	3
Caelo	Clobetasol propionate	1110116	1
Caelo	Clobetasol propionate	CL0024/0915	1
Caelo	Clobetasol propionate	CL0/1191217	1
Caelo	Clobetasol propionate	18300203	3
Caelo	Clobetasol propionate	16106709	16
Caelo	Clobetasol propionate	16C18-B02-325573	1
Caelo	Clobetasol propionate	15234002	1
Caelo	Clobetasol propionate	1438007	1
Caelo	Clobetasol propionate	1408018-02	10
Caelo	Clobetasol propionate	152340004	1
Caelo	Clobetasol propionate	15439501	6
Caelo	Clobetasol propionate	16106702	13
Caelo	Clobetasol propionate	16106711	23
Caelo	Clobetasol propionate	17096702	7
Caelo	Clobetasol propionate	17096706	17
Caelo	Clobetasol propionate	16353208	1
Caelo	Clobetasol propionate	1735603	1
Caelo	Clobetasol propionate	18300209	1
Caelo	Clobetasol propionate	3440	1
Caelo	Clobetasol propionate	13269510	2
Caelo	Clobetasol propionate	15A14-B02	1
Caelo	Clobetasol propionate	14338007	6
Caelo	Clobetasol propionate	16106703	18
Caelo	Clobetasol propionate	16G18-B02-324627	1
Caelo	Clobetasol propionate	17096701	8
Caelo	Clobetasol propionate	17097608	1
Caelo	Clobetasol propionate	14338008	5
Caelo	Clobetasol propionate	1524003	1
Caelo	Clobetasol propionate	17096705	14
Caelo	Clobetasol propionate	17096704	2
Caelo	Clobetasol propionate	17096708	23
Caelo	Clobetasol propionate	17325605	12
Caelo	Clobetasol propionate	15234003	17
Caelo	Clobetasol propionate	15C23-B02-310473	1
Caelo	Clobetasol propionate	17E04-B02-336882	1
Caelo	Clobetasol propionate	17L18-B02-347993	1
Caelo	Clobetasol propionate	18300212	2
Caelo	Clobetasol propionate	1606022	1
Caelo	Clobetasol propionate	17325606	4

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Supplier	Substance	Batch	Spectra
Caeolo	Clobetasol propionate	18040020108638392	1
Caeolo	Clobetasol propionate	17096709	1
Caeolo/Krieger	Clobetasol propionate	17096706	3
Caeolo/Noweda	Clobetasol propionate	15439503	1
Caesar & Loretz GmbH	Clobetasol propionate	18082710	1
Caesar & Loretz GmbH	Clobetasol propionate	18082711	1
Caesar & Loretz GmbH	Clobetasol propionate	18082709	1
Caesar & Loretz GmbH	Clobetasol propionate	18082718	2
Caesar & Loretz GmbH	Clobetasol propionate	18082708	1
Caesar & Loretz GmbH	Clobetasol propionate	18300204	3
Caesar & Loretz GmbH	Clobetasol propionate	18300208	3
Caesar & Loretz GmbH	Clobetasol propionate	18300202	1
Caesar & Loretz GmbH	Clobetasol propionate	18300210	1
Caesar & Loretz GmbH	Clobetasol propionate	18082703	1
Caesar & Loretz GmbH	Clobetasol propionate	18300209	1
Caesar & Loretz GmbH / ...	Clobetasol propionate	18082718	1
Caesar & Loretz GmbH/E ...	Clobetasol propionate	18082714	1
Caesar & Loretz/ Noweda	Clobetasol propionate	12342306	1
Caesar u Loretz	Clobetasol propionate	12107608	2
Caesar&Lorenz	Clobetasol propionate	1610370	1
Caesar&Loretz GmbH	Clobetasol propionate	15234001	1
Caesar&Loretz GmbH	Clobetasol propionate	15439501	1
Caesar/Lorenz	Clobetasol propionate	12342305	3
Caesar/Lorenz	Clobetasol propionate	12342309	1
Caesar/Loretz	Clobetasol propionate	12342310	1
Chiesi/ Now	Clobetasol propionate	13269503	3
Crystal Pharma	Clobetasol propionate	C0054/1	1
Delta	Clobetasol propionate	17096701	1
E Plus	Clobetasol propionate	16106702	1
EuRho	Clobetasol propionate	1408018-01	1
EuRho	Clobetasol propionate	1804002-01	1
EuRho 06.10.2011 Anzag	Clobetasol propionate	1108044-01	1
EuRho/ Phönix	Clobetasol propionate	1704020-01	1
EuRho/Gehe	Clobetasol propionate	1704020-01	1
EuRho/Phoenix	Clobetasol propionate	160602202	1
EuRho/Phoenix	Clobetasol propionate	1903014	1
Euro	Clobetasol propionate	1211021-02	2
euro AHD	Clobetasol propionate	1704020-015592	1
euro AHD	Clobetasol propionate	1804002-015788	1
Euro OT	Clobetasol propionate	14081018-02	1
Euro OTC	Clobetasol propionate	1704020-01	95
Euro OTC	Clobetasol propionate	1108044-037-16	1
Euro OTC	Clobetasol propionate	12110-01	1
Euro OTC	Clobetasol propionate	18111403	1
Euro OTC	Clobetasol propionate	140801801	1
Euro OTC	Clobetasol propionate	4091512	1
Euro OTC	Clobetasol propionate	160602201	6
Euro OTC	Clobetasol propionate	1606022-01	29
Euro OTC	Clobetasol propionate	1408018	1
Euro OTC	Clobetasol propionate	160602202	4
Euro OTC	Clobetasol propionate	16106720	1
Euro OTC	Clobetasol propionate	17096705	1
Euro OTC	Clobetasol propionate	1704020-015498	1
Euro OTC	Clobetasol propionate	18041808	1
Euro OTC	Clobetasol propionate	180400201	2
Euro OTC	Clobetasol propionate	18082703	2
Euro OTC	Clobetasol propionate	1804002201	1
Euro OTC	Clobetasol propionate	140808-02	1
Euro OTC	Clobetasol propionate	171107CP/1704020-01	1
Euro OTC	Clobetasol propionate	819081-39	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Clobetasol propionate	1606022-02	42
Euro OTC	Clobetasol propionate	1801002-01	1
Euro OTC	Clobetasol propionate	1108044-04	15
Euro OTC	Clobetasol propionate	CL0119/1217	1
Euro OTC	Clobetasol propionate	110804404	2
Euro OTC	Clobetasol propionate	1211021-01	19
Euro OTC	Clobetasol propionate	12082013B	1
Euro OTC	Clobetasol propionate	16042014C	1
Euro OTC	Clobetasol propionate	130604002	1
Euro OTC	Clobetasol propionate	30092014A	1
Euro OTC	Clobetasol propionate	1408018-01	15
Euro OTC	Clobetasol propionate	13042015A	1
Euro OTC	Clobetasol propionate	1072015D	1
Euro OTC	Clobetasol propionate	15234003	1
Euro OTC	Clobetasol propionate	17E04-B02-338441	1
Euro OTC	Clobetasol propionate	1408018-03	28
Euro OTC	Clobetasol propionate	1108044	1
Euro OTC	Clobetasol propionate	80616-1	1
Euro OTC	Clobetasol propionate	CL0-BLT223/1216	1
Euro OTC	Clobetasol propionate	1204037-01	1
Euro OTC	Clobetasol propionate	1108044-03	14
Euro OTC	Clobetasol propionate	1108044-02	8
Euro OTC	Clobetasol propionate	1105044-04	1
Euro OTC	Clobetasol propionate	1108044-01	4
Euro OTC	Clobetasol propionate	2111I-02835	1
Euro OTC	Clobetasol propionate	121102101	2
Euro OTC	Clobetasol propionate	1408015-01	1
Euro OTC	Clobetasol propionate	140801803	2
Euro OTC	Clobetasol propionate	1601046-01	1
Euro OTC	Clobetasol propionate	EuroOTC	4
Euro OTC	Clobetasol propionate	CL0-BL2153/0711	1
Euro OTC	Clobetasol propionate	1804002-01	69
Euro/ANZAG	Clobetasol propionate	1606022-02	1
Euro/ANZAG	Clobetasol propionate	1804002-01	1
euroho/gehe	Clobetasol propionate	1211021-01	1
Euro OTC	Clobetasol propionate	700225	2
Euro OTC	Clobetasol propionate	1704020	2
Euro OTC	Clobetasol propionate	4113Q-02835	1
Euro OTC	Clobetasol propionate	CL0-BL2322/1012	2
Euro OTC	Clobetasol propionate	1903014-01	9
Fagron	Clobetasol propionate	14G30-B07-302114	10
Fagron	Clobetasol propionate	16G18-B02-325571	2
Fagron	Clobetasol propionate	12E08-N04	11
Fagron	Clobetasol propionate	11-05-N06	1
Fagron	Clobetasol propionate	11L12-N05	2
Fagron	Clobetasol propionate	12J25-N01	3
Fagron	Clobetasol propionate	11/29-N07	1
Fagron	Clobetasol propionate	11D26-N04	1
Fagron	Clobetasol propionate	11H10-N02	1
Fagron	Clobetasol propionate	13A02-N04	18
Fagron	Clobetasol propionate	13G23N01	1
Fagron	Clobetasol propionate	13G23-N01	18
Fagron	Clobetasol propionate	3713M-02835	1
Fagron	Clobetasol propionate	12E08N04	1
Fagron	Clobetasol propionate	13Ao2-N04	1
Fagron	Clobetasol propionate	1211021-02	1
Fagron	Clobetasol propionate	1211021	1
Fagron	Clobetasol propionate	13K08-B30-287730	2
Fagron	Clobetasol propionate	13k08b30287728	1
Fagron	Clobetasol propionate	13K08B30287730	1

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Supplier	Substance	Batch	Spectra
Fagron	Clobetasol propionate	13K08-B30-287729	2
Fagron	Clobetasol propionate	13K08-B30-287727	1
Fagron	Clobetasol propionate	14G30-B07-302116	4
Fagron	Clobetasol propionate	15A14-B02-303125	10
Fagron	Clobetasol propionate	14C03-B07-305985	1
Fagron	Clobetasol propionate	14G30-B07-302112	1
Fagron	Clobetasol propionate	15a14-b02-303125	2
Fagron	Clobetasol propionate	1405018-02	1
Fagron	Clobetasol propionate	14C03-B07-305986	1
Fagron	Clobetasol propionate	15c23-b02-310473	2
Fagron	Clobetasol propionate	15H26-B03-312355	2
Fagron	Clobetasol propionate	15C23-B02-310473	2
Fagron	Clobetasol propionate	16E04-B12-322020	4
Fagron	Clobetasol propionate	16E04-B12	1
Fagron	Clobetasol propionate	16E04-B12-321033	2
Fagron	Clobetasol propionate	15j15-B04-317698	1
Fagron	Clobetasol propionate	16G18-B02-325573	8
Fagron	Clobetasol propionate	16H22-B07-330169	3
Fagron	Clobetasol propionate	1606022-02	1
Fagron	Clobetasol propionate	16G18-B02-325572	1
Fagron	Clobetasol propionate	16K24-B04-333121	1
Fagron	Clobetasol propionate	17E04-B02-335335	1
Fagron	Clobetasol propionate	17E04-B02-336882	2
Fagron	Clobetasol propionate	17G14-B12-341743	1
Fagron	Clobetasol propionate	17L18-B02-347992	1
Fagron	Clobetasol propionate	16k24-b04-332086	1
Fagron	Clobetasol propionate	17L18-B02-347993	3
Fagron	Clobetasol propionate	17L18B02-344841	1
Fagron	Clobetasol propionate	17L18-B02347991	1
Fagron	Clobetasol propionate	18/12-B02-354809	1
Fagron	Clobetasol propionate	18l12-B02-354809	1
Fagron	Clobetasol propionate	17L18-B02-351867	1
Fagron	Clobetasol propionate	18/12-B02-353202	2
Fagron	Clobetasol propionate	18l12-Bo2-353201	1
Fagron	Clobetasol propionate	18/12-B02-355657	1
Fagron	Clobetasol propionate	CL0103/0518	1
Fagron	Clobetasol propionate	18/12-B02-353202	2
Fagron	Clobetasol propionate	17L18-B02-347991	1
Fagron	Clobetasol propionate	18l12-B02-355065	1
Fagron	Clobetasol propionate	18/12-B02-355390	2
Fagron	Clobetasol propionate	18l12-B02-357669	1
Fagron	Clobetasol propionate	16G18-B02-32571	1
Fagron	Clobetasol propionate	16K24-B04-331220	1
Fagron	Clobetasol propionate	18/12-B02-355065	1
Fagron	Clobetasol propionate	17G14-B12-340175	6
Fagron	Clobetasol propionate	14G30-B07-302112	2
Fagron	Clobetasol propionate	1314705	1
Fagron	Clobetasol propionate	18l12-B02-353203	1
Fagron	Clobetasol propionate	18/12-B02-353201	1
Fagron	Clobetasol propionate	14C03-B07-293563	1
Fagron	Clobetasol propionate	18I12-B02-353202	1
Fagron	Clobetasol propionate	15C23-B02-310522	2
Fagron	Clobetasol propionate	15J15-B04-317698	6
Fagron	Clobetasol propionate	16K24-B04-332086	6
Fagron	Clobetasol propionate	14G30-B07-302113	2
Fagron	Clobetasol propionate	12A02-N04	1
Fagron	Clobetasol propionate	16K24-B04-333120	1
Fagron	Clobetasol propionate	17L18-B02-345404	2
Fagron	Clobetasol propionate	14G30-B07-302115	2
Fagron	Clobetasol propionate	18I12-B02-355390	1

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Supplier	Substance	Batch	Spectra
Fagron	Clobetasol propionate	15C23-B02-310473	12
Fagron	Clobetasol propionate	14C03-B07-293560	1
Fagron	Clobetasol propionate	16E04-B12-321036	1
Fagron	Clobetasol propionate	1704020-01	4
Fagron	Clobetasol propionate	18I12-B02-355391	2
Fagron	Clobetasol propionate	13G23-N01	1
Fagron	Clobetasol propionate	15G01-B02-311578	1
Fagron	Clobetasol propionate	17E04-B02-338441	3
Fagron	Clobetasol propionate	17G14-B12-340176	3
Fagron	Clobetasol propionate	11C16-N01	1
Fagron	Clobetasol propionate	15H26-B03-312860	1
Fagron	Clobetasol propionate	11I29-N07	1
Fagron	Clobetasol propionate	16G18B02325571	1
Fagron	Clobetasol propionate	16K24-B04-333120	5
Fagron	Clobetasol propionate	CL0101/0417	1
Fagron	Clobetasol propionate	17E04B02336882	1
Fagron	Clobetasol propionate	17L18B02347991	1
Fagron	Clobetasol propionate	14C03-B07-293561	2
Fagron	Clobetasol propionate	14C03-B07	2
Fagron	Clobetasol propionate	16K24-B04-333143	4
Fagron	Clobetasol propionate	17096708	1
Fagron	Clobetasol propionate	19B06-B03-60603	1
Fagron	Clobetasol propionate	16E04-B12-321032	1
Fagron	Clobetasol propionate	13K08-B30-287726	2
Fagron	Clobetasol propionate	13K08-B03-287728	1
Fagron	Clobetasol propionate	15J15-B04	1
Fagron	Clobetasol propionate	16G18-B02-324627	5
Fagron	Clobetasol propionate	16K24B04333121	1
Fagron	Clobetasol propionate	NS0486M	1
Fagron	Clobetasol propionate	13G23-N01NT0421M	1
Fagron	Clobetasol propionate	13K08-B30-287728	5
Fagron	Clobetasol propionate	13K08-B30	2
Fagron	Clobetasol propionate	16K24-B04	1
Fagron	Clobetasol propionate	18I12-B02	1
Fagron	Clobetasol propionate	14C03-B07-305987	2
Fagron	Clobetasol propionate	15/15-B04-317699	1
Fagron	Clobetasol propionate	16H22-B07-328012	11
Fagron	Clobetasol propionate	16106704	1
Fagron	Clobetasol propionate	17L18-B02-344842	3
Fagron	Clobetasol propionate	15J15-B04-316615	1
Fagron	Clobetasol propionate	NS0292-M	1
Fagron	Clobetasol propionate	14C03-B07-293562	9
Fagron	Clobetasol propionate	14G30-B07-303114	1
Fagron	Clobetasol propionate	18I12-B02-353202	1
Fargon	Clobetasol propionate	14C03-B07	1
Fargon/Phoenix 23.01.2018	Clobetasol propionate	17E04-B02-338441	1
Farmabios S.p.A./Caesar...	Clobetasol propionate	14338006	1
Fgaron	Clobetasol propionate	15H26-B03	1
Fiebig	Clobetasol propionate	1804002-01	1
Finteler Apotheke	Clobetasol propionate	16K24-B04-333121	2
Fischar	Clobetasol propionate	14188506	1
gehe	Clobetasol propionate	APCLPM03616C	1
Gehe	Clobetasol propionate	10D21-N04	1
Gehe	Clobetasol propionate	12107606	1
Gehe	Clobetasol propionate	12342306	2
Gehe	Clobetasol propionate	12342310	1
Gehe	Clobetasol propionate	12J25-N01	1
Gehe	Clobetasol propionate	14188504	1
Gehe	Clobetasol propionate	15234003	1
Gehe	Clobetasol propionate	1606022-01	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Gehe	Clobetasol propionate	16106704	1
Gehe	Clobetasol propionate	16106701	1
Gehe	Clobetasol propionate	17096705	1
Gehe	Clobetasol propionate	1704020-01	1
Gehe	Clobetasol propionate	17096708	1
Gehe	Clobetasol propionate	18082703	1
Gehe	Clobetasol propionate	18I12-B02-355391	1
Gehe	Clobetasol propionate	18I12-B02-353203	1
GEHE	Clobetasol propionate	16G18-B02-324627	1
GEHE	Clobetasol propionate	17096707	1
GEHE 21.03.2014	Clobetasol propionate	1211021-02	1
Caelo	Clobetasol propionate	ap1/294/b-14	1
Caelo	Clobetasol propionate	15439503	21
Caelo	Clobetasol propionate	1070317/16106704	1
Caelo	Clobetasol propionate	17096706/1180418	1
Caelo	Clobetasol propionate	160602201	1
HCK	Clobetasol propionate	11/05-N06	1
Hedinger/ Sanacorp	Clobetasol propionate	APAPL/035/E-12C	1
Henry Lamotte	Clobetasol propionate	16106704	1
Heyl/Noweda	Clobetasol propionate	15234001	2
Ichtyol / Noweda	Clobetasol propionate	17325605	1
Jenne	Clobetasol propionate	17325601	2
Caelo	Clobetasol propionate	8082703	1
L10	Clobetasol propionate	16106703	2
L10	Clobetasol propionate	18082708	1
L12	Clobetasol propionate	16106711	1
L12	Clobetasol propionate	17325602	1
Midas	Clobetasol propionate	16106704	2
Midas	Clobetasol propionate	17096705	1
Nachprüfung vom 19.06.17	Clobetasol propionate	9302004	2
Noweda	Clobetasol propionate	11300702	1
Noweda	Clobetasol propionate	12342305	1
Noweda	Clobetasol propionate	12342310	1
Noweda	Clobetasol propionate	13134701	1
Noweda	Clobetasol propionate	13134705	1
Noweda	Clobetasol propionate	14338007	1
Noweda	Clobetasol propionate	15234004	1
Noweda	Clobetasol propionate	16106720	1
Noweda	Clobetasol propionate	1606022-02	1
Noweda	Clobetasol propionate	17096706	1
Noweda	Clobetasol propionate	17325605	1
Caelo	Clobetasol propionate	13K08-B30-287728	1
Caelo	Clobetasol propionate	1704020	1
Noweda 6.4.17	Clobetasol propionate	1606022-01	1
Noweda/ Ichthyol	Clobetasol propionate	15439503	1
Noweda/Anzag	Clobetasol propionate	13269504	3
Noweda/Apomix	Clobetasol propionate	16106703	1
Noweda/EuRo	Clobetasol propionate	1606022-01	1
Oberlinden Apotheke	Clobetasol propionate	B0054/116010Mg60g	1
Euro OTC	Clobetasol propionate	170402001	8
Euro OTC	Clobetasol propionate	c1o-b1t223/126	1
Euro OTC	Clobetasol propionate	14080-02	1
Euro OTC	Clobetasol propionate	121K021-01	1
Phoenix	Clobetasol propionate	13K08B30287728	1
Phoenix	Clobetasol propionate	15439502	1
Phoenix	Clobetasol propionate	16h22-b07-328012	1
Phoenix	Clobetasol propionate	16H-B07-330169	1
Phoenix	Clobetasol propionate	3063	1
Phoenix	Clobetasol propionate	1704020-01	1
Phoenix	Clobetasol propionate	18082703	2

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Supplier	Substance	Batch	Spectra
Phoenix	Clobetasol propionate	1804002-01	1
Phoenix	Clobetasol propionate	3365	1
Phoenix	Clobetasol propionate	3366	1
Phoenix	Clobetasol propionate	18082709	1
Phoenix 02.04.2014	Clobetasol propionate	1211021-03	3
Phoenix 29.11.12	Clobetasol propionate	700225	2
Phoenix WE 29.04.17 -15...	Clobetasol propionate	1606022-02	1
Caelo	Clobetasol propionate	1610670	1
Caelo	Clobetasol propionate	16106720	7
Phoenix/Cealo	Clobetasol propionate	17096701	1
phönix	Clobetasol propionate	15439503	1
phönix	Clobetasol propionate	15439504	1
phönix	Clobetasol propionate	16106704	1
Phönix	Clobetasol propionate	13134701	1
Phönix	Clobetasol propionate	16106703	1
Phönix	Clobetasol propionate	17096706	1
Phönix	Clobetasol propionate	3161	1
Phönix	Clobetasol propionate	3182	1
Fagron	Clobetasol propionate	17G14-B12-341742	1
Phönix Caesar u. Loretz	Clobetasol propionate	13269508	1
Phönix Gotha	Clobetasol propionate	1108044-04	1
Phönix Gotha	Clobetasol propionate	1211021-02	3
phönix herne	Clobetasol propionate	180400201	1
Caelo	Clobetasol propionate	121102104	1
Caelo	Clobetasol propionate	16106712	4
Phönix/Euro	Clobetasol propionate	1804002-01	1
PhönixWE24.10.2014 EK...	Clobetasol propionate	1211021-04	1
Raben-Apotheke Mildenau	Clobetasol propionate	13k08-b30-287727	1
Caelo	Clobetasol propionate	12342310	7
sanacorp	Clobetasol propionate	13269508	1
sanacorp	Clobetasol propionate	14188506	1
Sanacorp	Clobetasol propionate	1108044-03	1
Sanacorp	Clobetasol propionate	12107608	1
Sanacorp	Clobetasol propionate	12107609	2
Sanacorp	Clobetasol propionate	1211021-01	1
Sanacorp	Clobetasol propionate	12342310	1
Sanacorp	Clobetasol propionate	13g23n01	1
Sanacorp	Clobetasol propionate	13269507	1
Sanacorp	Clobetasol propionate	15234003	1
Sanacorp	Clobetasol propionate	1606022-02	2
Caelo	Clobetasol propionate	14188503	17
Caelo	Clobetasol propionate	18300204	3
Caelo	Clobetasol propionate	12J25-N01	1
Caelo	Clobetasol propionate	36/AKD2	1
Fagron	Clobetasol propionate	11300703	1
Fagron	Clobetasol propionate	17L18-B02-345403	2
Sanacorp;19.03.15;87,60EUR	Clobetasol propionate	14C03-B07-293563	1
Symbiotica / Noweda	Clobetasol propionate	1704020-01	1
Symbiotica Spec.	Clobetasol propionate	1211021-03	1
Symbiotica Spec./Phönix	Clobetasol propionate	CL0-B12153/0711	1
Symbiotica Spec./Phönix	Clobetasol propionate	1108044-04	1
symbiotica/gehe	Clobetasol propionate	1211021-03	1
Symbiotica/Phönix	Clobetasol propionate	1408018-02	1
Symbiotica/Sanacorp	Clobetasol propionate	1408018-03	1
Symbiotitica/Noweda	Clobetasol propionate	1606022-01	1
Caelo	Clobetasol propionate	12107601	3
Caelo	Clobetasol propionate	12107602	3
WE: 20.01.16	Clobetasol propionate	15234004	1
Euro OTC	Clobetasol propionate	1211021-04	21
Caelo	Clobetasol propionate	13134705	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Clobetasol propionate	14338001	9
Caelo	Clobetasol propionate	15439504	25
Caelo	Clobetasol propionate		1
Caelo	Clobetasol propionate	13269505	1
Euro OTC	Clobetasol propionate	1606022	3
	Clobetasol propionate	11/29-N07	1
Phönix	Clobetasol propionate		1

- 109 321 spectra from 741 *Apo-Ident* customers from a total of 31 528 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clobetasol propionate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clobetasol propionate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	656	4	110 029
Type B	0	516	14	118 612
Type C	0	1788	138	109 321

The substance/substance group *Clobetasol propionate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	99.3939 % (> 98.9394 %)
Type B	100.0000 % (> 99.9893 %)	97.3585 % (> 96.7925 %)
Type C	100.0000 % (> 99.8899 %)	92.8349 % (> 92.6791 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Clobetasol propionate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Betamethasone dipropionate, micronized	10.25	48.21
Beclometasone dipropionate	20.83	54.07
Dexamethasone acetate	25.52	—
Betamethasone valerate	39.91	—
Triamcinolone acetonide	42.27	—
Dexamethasone	46.09	—
Lidocaine	50.30	—
⋮	⋮	⋮
Oxybutynin hydrochloride	>50	52.69
Gentamicin sulfate	>50	222.83
Sodium citrate	>50	411.30
Sodium benzoate	>50	590.81

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Clobetasol propionate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22724	21092	3.77	10.25
21802	21802	0.00	15.44
21611	21611	0.00	15.18
22714	22714	0.00	13.57
24691	22714	7.20	15.64
21092	21092	0.00	11.58
21473	21473	0.00	16.19
21896	21896	0.00	10.27
24904	24904	0.00	11.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Clonidine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20637-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Clonidine hydrochloride; Clonidini hydrochloridum

Special notes

When selecting the *Clonidine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Clonidine hydrochloride	3	2	3

Second-stage model

For differentiation of the substance/substance group *Clonidine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Clonidine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Clonidine hydroc...	13I25-B07	21220	40	20131009
Fagron	Clonidine hydroc...	14H11-B04-311163	21966	60	AR-18-FG-006797-02
Fagron	Clonidine hydroc...	14H11-B04-311163	22967	40	20140929
Fagron	Clonidine hydroc...	14H11-B04-311163	22967SI	40	20140929
Fagron	Clonidine hydroc...	19B27-B02-361777	24687	40	20190607

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Clonidine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 469 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 340 spectra of 8 reference samples from the substance/substance group *Clonidine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Clonidine hydrochloride	15L11-B01-332270	23228	40
Fagron	Clonidine hydrochloride	18B12-B04-353341	24443	40
Fagron	Clonidine hydrochloride	14H11-B04-311163	21966SI [†]	60
Fagron	Clonidine hydrochloride	15L11-B01-332270	23228SI	40
Fagron	Clonidine hydrochloride	15L11-B01-332270	23410	40
Fagron	Clonidine hydrochloride	15L11-B01-332270	23410SI	40
Fagron	Clonidine hydrochloride	18B12-B04-353341	24443SI	40
Fagron	Clonidine hydrochloride	19B27-B02-361777	24687SI [†]	40

- 118 802 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 45 spectra from 7 *Apo-Ident* customers from 4 batches from the substance/substance group *Clonidine hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Clonidine hydrochloride	14H11-B04-298642	1
Fagron	Clonidine hydrochloride	15L11-B01	1
Fagron	Clonidine hydrochloride	18B12-B04-353341	1
Fagron	Clonidine hydrochloride	14H11-B04-311163	42

- 111 202 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clonidine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clonidine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	339	1	118 802
Type C	0	45	0	111 202

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

The substance/substance group *Clonidine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	99.7059 % (> 98.8235 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 86.6667 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Clonidine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	58.20	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Clonidine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21220	21966	8.92	60.50
21966	21966	0.00	61.58
22967	21966	13.63	57.27
24687	21966	16.08	56.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Clotrimazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20000-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Clotrimazole; Clotrimazolum

Special notes

When selecting the *Clotrimazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Clotrimazole	9	9	501

Second-stage model

For differentiation of the substance/substance group *Clotrimazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Clotrimazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Clotrimazole	13184113	21087	40	20130614
Caelo	Clotrimazole	13224204	21114	40	20130815
Caelo	Clotrimazole	13224220	21352	40	20130815
Caelo	Clotrimazole	13224220	21353	40	20130815
Caelo	Clotrimazole	153956	23791	40	20151215*
Euro OTC	Clotrimazole	1306036-01	21207	40	20130823
Euro OTC	Clotrimazole	1510003	22229	60	20151111*
Fagron	Clotrimazole	12I21-N01	20794	40	20120322
Fagron	Clotrimazole	14B05-B36	21259	40	20140225
Fagron	Clotrimazole	14C04-B31	21264	40	20140319

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 420 spectra of 10 reference samples from the substance/substance group *Clotrimazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 269 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 350 spectra of 9 reference samples from the substance/substance group *Clotrimazole*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Clotrimazole	12320815	20861	30
Caelo	Clotrimazole	171116	23322	40
Caelo	Clotrimazole	17111616	23781	40
Caelo	Clotrimazole	190161	24512	40
Caelo	Clotrimazole	190162	24517	40
Euro OTC	Clotrimazole	1607046	22793	40
Euro OTC	Clotrimazole	1703028	23129	40
Euro OTC	Clotrimazole	1808028	24298	40
Euro OTC	Clotrimazole	1902004	24461	40

- 118 792 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2885 spectra from 626 *Apo-Ident* customers from 532 batches from the substance/substance group *Clotrimazole*.
- Among them are spectra of independent samples from 499 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H.D.	Clotrimazole	14337801	1
AHD	Clotrimazole	13184105	1
AHD	Clotrimazole	1703028-03	1
AHD	Clotrimazole	1808028-01	1
AHD	Clotrimazole	1902004-01	1
Caelo	Clotrimazole	17360203	11
Caelo	Clotrimazole	18147216	3
AHD 27.10 Ek.7,07	Clotrimazole	1607046	1
Caelo	Clotrimazole	14B05-B35	1
Fagron	Clotrimazole	15G14-B06-311054	4
AHD/Hedinger	Clotrimazole	14337807	1
Fagron	Clotrimazole	15G14-B05-311102	4
Fagron	Clotrimazole	14C04-B31-299959	2
Alliance Healthcare	Clotrimazole	1309034-01	1
Alliance Healthcare	Clotrimazole	AP1510003-01C	1
Alliance Healthcare	Clotrimazole	18147216	1
Fagron	Clotrimazole	16J07B02341842	2
Fagron	Clotrimazole	18A18B05352114	1
Alliance/Euro	Clotrimazole	1703028-01	1
Anzag	Clotrimazole	14C04-B30-2916618	1
Anzag	Clotrimazole	15G14-B06	1
Anzag	Clotrimazole	15395610	1

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Supplier	Substance	Batch	Spectra
Anzag	Clotrimazole	1703028-01	1
Fagron	Clotrimazole	20120603	3
Euro OTC	Clotrimazole	1510003-02	22
Fagron	Clotrimazole	16J07-B02-335773	1
apo ident	Clotrimazole	1607046-02	1
Apomix	Clotrimazole	14B05-B36	1
apomix/Phönix	Clotrimazole	15G14-B05-311103	3
Audor Pharma	Clotrimazole	APCLT/1703/0016CC	3
Audor Pharma	Clotrimazole	APCLT/1703/0016C	1
Audor Pharma	Clotrimazole	AP1306036-01C	1
Audor Pharma	Clotrimazole	1703028-02	1
Audor Pharma	Clotrimazole	1703/0016CC	1
Bombastus	Clotrimazole	Validierungsmessung	1
Bombastus	Clotrimazole	14337817	1
Bombastus	Clotrimazole	12320815	1
Bombastus	Clotrimazole	17360203	1
Caello/Anzag	Clotrimazole	14337815	1
Caelo	Clotrimazole	14c04-b31-299954	2
Caelo	Clotrimazole	11-K21-N19	1
Caelo	Clotrimazole	20111115	1
Caelo	Clotrimazole	12159904	2
Caelo	Clotrimazole	11305511	1
Caelo	Clotrimazole	12E02-N12	2
Caelo	Clotrimazole	12320807	4
Caelo	Clotrimazole	20111018	1
Caelo	Clotrimazole	12320809	4
Caelo	Clotrimazole	12320808	11
Caelo	Clotrimazole	1259913	1
Caelo	Clotrimazole	1234567	1
Caelo	Clotrimazole	12B27-N05	2
Caelo	Clotrimazole	13184103	10
Caelo	Clotrimazole	26071305	1
Caelo	Clotrimazole	12320815	1
Caelo	Clotrimazole	11305507	1
Caelo	Clotrimazole	311111	1
Caelo	Clotrimazole	131841111	1
Caelo	Clotrimazole	13224211	5
Caelo	Clotrimazole	1322401	1
Caelo	Clotrimazole	11081201	1
Caelo	Clotrimazole	13224212	8
Caelo	Clotrimazole	412091-2-P	1
Caelo	Clotrimazole	13224214	9
Caelo	Clotrimazole	13224216	9
Caelo	Clotrimazole	156546	1
Caelo	Clotrimazole	13224217	9
Caelo	Clotrimazole	415050-2-P	1
Caelo	Clotrimazole	13324204	1
Caelo	Clotrimazole	1306036	1
Caelo	Clotrimazole	13224218	12
Caelo	Clotrimazole	418072-1-P	1
Caelo	Clotrimazole	14144905	17
Caelo	Clotrimazole	132243218	1
Caelo	Clotrimazole	1309034-02	3
Caelo	Clotrimazole	14144912	2
Caelo	Clotrimazole	14144911	13
Caelo	Clotrimazole	14C04-B30-291656	2
Caelo	Clotrimazole	14144918	12
Caelo	Clotrimazole	14144917	5
Caelo	Clotrimazole	14C04-B32-291657	1
Caelo	Clotrimazole	14144913	2

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Supplier	Substance	Batch	Spectra
Caelo	Clotrimazole	14337802	8
Caelo	Clotrimazole	14337807	9
Caelo	Clotrimazole	143337811	1
Caelo	Clotrimazole	14337815	10
Caelo	Clotrimazole	14337813	6
Caelo	Clotrimazole	14337817	14
Caelo	Clotrimazole	14337829	19
Caelo	Clotrimazole	17011601	1
Caelo	Clotrimazole	14337824	3
Caelo	Clotrimazole	15G14-B06-311057	1
Caelo	Clotrimazole	1409027-04	1
Caelo	Clotrimazole	14337818	10
Caelo	Clotrimazole	310316-5-461	1
Caelo	Clotrimazole	14337827	10
Caelo	Clotrimazole	15395602	17
Caelo	Clotrimazole	14337830	3
Caelo	Clotrimazole	1510003-01	4
Caelo	Clotrimazole	15395605	14
Caelo	Clotrimazole	14B05-B36-291168	1
Caelo	Clotrimazole	141104C	1
Caelo	Clotrimazole	15395611	10
Caelo	Clotrimazole	1539613	1
Caelo	Clotrimazole	15395615	6
Caelo	Clotrimazole	1607046-01	6
Caelo	Clotrimazole	15295603	1
Caelo	Clotrimazole	15395617	9
Caelo	Clotrimazole	15395618	17
Caelo	Clotrimazole	16234503	13
Caelo	Clotrimazole	16B11-B04-322393	1
Caelo	Clotrimazole	16234505	21
Caelo	Clotrimazole	1623455	1
Caelo	Clotrimazole	160704601	1
Caelo	Clotrimazole	15395623	2
Caelo	Clotrimazole	16234513	18
Caelo	Clotrimazole	16234502	5
Caelo	Clotrimazole	1170717	1
Caelo	Clotrimazole	1703028-01	6
Caelo	Clotrimazole	162345135319	1
Caelo	Clotrimazole	16234517	5
Caelo	Clotrimazole	14101716	1
Caelo	Clotrimazole	17111604	8
Caelo	Clotrimazole	17111605	16
Caelo	Clotrimazole	17111604	2
Caelo	Clotrimazole	17111612	1
Caelo	Clotrimazole	16J07-B02	1
Caelo	Clotrimazole	17111613	19
Caelo	Clotrimazole	17111606	1
Caelo	Clotrimazole	17111615	14
Caelo	Clotrimazole	162345225555	1
Caelo	Clotrimazole	17111608	10
Caelo	Clotrimazole	17360202	21
Caelo	Clotrimazole	14337824NP	1
Caelo	Clotrimazole	1703028-03	1
Caelo	Clotrimazole	18147201	1
Caelo	Clotrimazole	171113608	1
Caelo	Clotrimazole	17/25-B06-345048	1
Caelo	Clotrimazole	17260204	1
Caelo	Clotrimazole	17360204	15
Caelo	Clotrimazole	18147101	26
Caelo	Clotrimazole	18147203	26

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Supplier	Substance	Batch	Spectra
Caelo	Clotrimazole	1808028-01	1
Caelo	Clotrimazole	18147212	7
Caelo	Clotrimazole	19016103	7
Caelo	Clotrimazole	1916202	1
Caelo	Clotrimazole	19016203	1
Caelo	Clotrimazole	18147217	4
Caelo	Clotrimazole	19016106	10
Caelo	Clotrimazole	19016107	7
Caelo	Clotrimazole	12I21-N04	1
Caelo	Clotrimazole	1210039-01	1
Caelo	Clotrimazole	16234506	1
Caelo	Clotrimazole	16J07-B02-330216	2
Caelo	Clotrimazole	16J07-B02-344818	2
Caelo	Clotrimazole	18A18-B05-347865	1
Caelo	Clotrimazole	18147208	1
Caelo	Clotrimazole	17111606	20
Caelo	Clotrimazole	14337812	7
Caelo	Clotrimazole	19016105	7
Caelo	Clotrimazole	1409027-03	3
Caelo	Clotrimazole	132234216	1
Caelo	Clotrimazole	Fagron	1
Caelo	Clotrimazole	1711161	1
Caelo	Clotrimazole	19B14-B01-359537	1
Caelo	Clotrimazole	12159911	2
Caelo	Clotrimazole	13184111	7
Caelo	Clotrimazole	15395604	13
Caelo	Clotrimazole	13224219	6
Caelo	Clotrimazole	12320814	9
Caelo	Clotrimazole	12E30-N07	1
Caelo	Clotrimazole	700135-0006	1
Caelo	Clotrimazole	17J25-B06-345045	1
Caelo	Clotrimazole	16051913	1
Caelo	Clotrimazole	15395613	8
Caelo	Clotrimazole	1901606	1
Caelo	Clotrimazole	14C04-B31-294939	1
Caelo	Clotrimazole	14337811	4
Caelo	Clotrimazole	13184105	12
Caelo	Clotrimazole	1902004-01	1
Caelo	Clotrimazole	17360201	20
Caelo	Clotrimazole	3335	1
Caelo	Clotrimazole	PC85	1
Caelo	Clotrimazole	17111601	9
Caelo	Clotrimazole	5117E-01276	1
Caelo	Clotrimazole	1210030-02	1
Caelo	Clotrimazole	18147102	20
Caelo	Clotrimazole	1306036-01	3
Caelo	Clotrimazole	15395603	9
Caelo	Clotrimazole	181471035763	1
Caelo	Clotrimazole	AP1510003-01C	1
Caelo	Clotrimazole	1906106	1
Caelo	Clotrimazole	1882321	2
Caelo	Clotrimazole	15G14-B06-311054	1
Caelo	Clotrimazole	16J07-B02_330236	1
Caelo	Clotrimazole	16234515	1
Caelo	Clotrimazole	16234522	10
Caelo	Clotrimazole	14337828	10
Caelo	Clotrimazole	13224225	2
Caelo	Clotrimazole	12159916	6
Caelo	Clotrimazole	13224210	11
Caelo	Clotrimazole	1309034-C1	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Clotrimazole	13224215	3
Caelo	Clotrimazole	160614	1
Caelo	Clotrimazole	14337816	16
Caelo	Clotrimazole	1437816	1
Caelo	Clotrimazole	16234509	9
Caelo	Clotrimazole	1150817/16234512	1
Caelo	Clotrimazole	17111616	20
Caelo	Clotrimazole	19016202	3
Caelo	Clotrimazole	12159902	11
Caelo	Clotrimazole	12159913	9
Caelo	Clotrimazole	13224201	21
Caelo	Clotrimazole	15G14-B05-316483	2
Caelo	Clotrimazole	14c04-B31	1
Caelo	Clotrimazole	19016119	5
Caelo	Clotrimazole	16234523	1
Caelo	Clotrimazole	1711613	2
Caelo	Clotrimazole	14337819	6
Caelo	Clotrimazole	14337801	13
Caelo	Clotrimazole	16E20-B10	2
Caelo	Clotrimazole	16234501	7
Caelo	Clotrimazole	16234511	13
Caelo	Clotrimazole	16234512	16
Caelo	Clotrimazole	20160801	2
Caelo	Clotrimazole	16234520	17
Caelo	Clotrimazole	17053186	1
Caelo	Clotrimazole	170302803	1
Caelo	Clotrimazole	18147206	1
Caelo	Clotrimazole	18147211	21
Caelo	Clotrimazole	14337809	14
Caelo	Clotrimazole	14C04B31-299954	1
Caelo	Clotrimazole	14C04-B31-299955	1
Caelo	Clotrimazole	15G14-B05-311101	1
Caelo	Clotrimazole	153965604	1
Caelo	Clotrimazole	16E20-B10-324555	1
Caelo	Clotrimazole	16B09B06311506	1
Caelo	Clotrimazole	16J07-B02-329385	3
Caelo	Clotrimazole	1711605	1
Caelo	Clotrimazole	18147103	14
Caelo	Clotrimazole	18147210	19
Caelo	Clotrimazole	18A18-B05-349662	1
Caelo	Clotrimazole	19016108	2
Caelo	Clotrimazole	19016116	4
Caelo	Clotrimazole	14B05-B36-291167	1
Caelo	Clotrimazole	14337832	1
Caelo	Clotrimazole	15395614	8
Caelo	Clotrimazole	15395610	6
Caelo	Clotrimazole	16234504	10
Caelo	Clotrimazole	1607046-02	5
Caelo	Clotrimazole	16B11-B04-325221	1
Caelo	Clotrimazole	16234521	5
Caelo	Clotrimazole	16J07-B02-329386	1
Caelo	Clotrimazole	2217Q-01276	1
Caelo	Clotrimazole	16B09-B06-311785	1
Caelo	Clotrimazole	1539561	1
Caelo	Clotrimazole	1711603	2
Caelo	Clotrimazole	1711816	1
Caelo	Clotrimazole	17A19-B04-340476	1
Caelo	Clotrimazole	18081408	1
Caelo	Clotrimazole	12320806	5
Caelo	Clotrimazole	12320813	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Clotrimazole	17111617	4
Caecolo/Gehe	Clotrimazole	16234521	1
Caesar & Loretz	Clotrimazole	16234504	1
Caesar & Loretz GmbH	Clotrimazole	17111604	1
Caesar & Loretz GmbH	Clotrimazole	17360204	2
Caesar & Loretz GmbH	Clotrimazole	16J07B02344817	1
Caesar & Loretz GmbH	Clotrimazole	18147210	5
Caesar & Loretz GmbH	Clotrimazole	18147103	1
Caesar & Loretz GmbH	Clotrimazole	18147216	1
Caesar & Loretz GmbH	Clotrimazole	18147211	1
Caesar & Loretz GmbH	Clotrimazole	19016105	2
Caesar & Loretz GmbH	Clotrimazole	19016108	5
Caesar & Loretz GmbH	Clotrimazole	19016106	2
Caesar & Loretz GmbH	Clotrimazole	19016119	3
Caesar & Loretz GmbH	Clotrimazole	19016116	2
Caesar & Loretz GmbH	Clotrimazole	19016208	3
Caesar & Loretz GmbH / ...	Clotrimazole	19016202	2
Caesar & Loretz GmbH, A...	Clotrimazole	18147203	1
Caesar & Loretz GmbH/Fi...	Clotrimazole	19016106	1
Caesar & Loretz GmbH/go...	Clotrimazole	19016105	1
Caesar & Loretz GmbH/go...	Clotrimazole	19016203	1
Caesar & Loretz/Sanacorp	Clotrimazole	18147210	1
Caesar u Loretz	Clotrimazole	15395613	1
Caesar u Loretz	Clotrimazole	16234501	1
Caesar&Lorenz / Gehe	Clotrimazole	19016199	1
Caesar&Loretz GmbH	Clotrimazole	14337814	1
Caesar&Loretz GmbH,15.0...	Clotrimazole	16234509	1
caesar&lorenz GmbH,Phön...	Clotrimazole	15395614	1
Caesar&Loretz GmbH/ San...	Clotrimazole	16234522	1
Caesar&Loretz GmbH/Anzag	Clotrimazole	13184111	1
Caesar&Loretz GmbH/Anzag	Clotrimazole	14337807	1
Caesar&lorenz,Phoenix	Clotrimazole	14144912	1
Caesar&LoretzGmbH, Phoe...	Clotrimazole	18147212	1
Caesar/Lorenz	Clotrimazole	12320814	1
Caesar/Lorenz	Clotrimazole	13224201	3
Cealo	Clotrimazole	17111612	1
Cealo/GEHE	Clotrimazole	18147101	2
Delta	Clotrimazole	1607046-01	1
Dr. Wolff	Clotrimazole	1409027-04	2
E Plus	Clotrimazole	1703028-02	1
E Plus	Clotrimazole	1808028-01	2
eurho	Clotrimazole	1309034-02	2
Eurho	Clotrimazole	1703028-02	1
EuRho	Clotrimazole	1108053-02	1
EuRho	Clotrimazole	1203040-02	2
EuRho	Clotrimazole	1203040-03	1
EuRho	Clotrimazole	1306036-01	2
EuRho	Clotrimazole	1210039-02	2
EuRho	Clotrimazole	1309034-02	1
EuRho	Clotrimazole	1409027-01	2
EuRho / Phoenix	Clotrimazole	1703028-01	1
EuRho AHC	Clotrimazole	1306036-01	1
EuRho/ Phoenix	Clotrimazole	160704602	1
EuRho/Kehr	Clotrimazole	1703028-02	1
EuRho/Phoenix	Clotrimazole	1210039-02	1
EuRho/Phoenix	Clotrimazole	1409027-01	1
EuRho/Phönix	Clotrimazole	1210039-2	1
EuRho/Sanacorp	Clotrimazole	16234522	1
Euro	Clotrimazole	1510003-01	2
Euro	Clotrimazole	160704601	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OT/Gehe	Clotrimazole	1409027-03	2
Euro OTC	Clotrimazole	20160801	4
Euro OTC	Clotrimazole	2881	1
Euro OTC	Clotrimazole	1108053-02	2
Euro OTC	Clotrimazole	1209211276	1
Euro OTC	Clotrimazole	1105014-01	1
Euro OTC	Clotrimazole	3912E-01276	1
Euro OTC	Clotrimazole	2313M01276	1
Euro OTC	Clotrimazole	1210039-02	22
Euro OTC	Clotrimazole	30011402	1
Euro OTC	Clotrimazole	1306306-01	1
Euro OTC	Clotrimazole	130603601	3
Euro OTC	Clotrimazole	1309034-01	21
Euro OTC	Clotrimazole	130903401	5
Euro OTC	Clotrimazole	130903402	1
Euro OTC	Clotrimazole	1409027-01	27
Euro OTC	Clotrimazole	23121408	1
Euro OTC	Clotrimazole	140902701	1
Euro OTC	Clotrimazole	1409027-02	41
Euro OTC	Clotrimazole	15010003-01	1
Euro OTC	Clotrimazole	2785	1
Euro OTC	Clotrimazole	1510003_01	1
Euro OTC	Clotrimazole	151000301	1
Euro OTC	Clotrimazole	H20160502	1
Euro OTC	Clotrimazole	16234504	1
Euro OTC	Clotrimazole	1703028-01	77
Euro OTC	Clotrimazole	170302801	6
Euro OTC	Clotrimazole	13418014	1
Euro OTC	Clotrimazole	1808028-01	59
Euro OTC	Clotrimazole	160802801	1
Euro OTC	Clotrimazole	1808028	3
Euro OTC	Clotrimazole	180002801	1
Euro OTC	Clotrimazole	1808028-02	34
Euro OTC	Clotrimazole	1703028-02	1
Euro OTC	Clotrimazole	1703028	1
Euro OTC	Clotrimazole	1306036	1
Euro OTC	Clotrimazole	170615C/1703028-01	1
Euro OTC	Clotrimazole	150003-02	1
Euro OTC	Clotrimazole	1409027-03	22
Euro OTC	Clotrimazole	16074046-01	1
Euro OTC	Clotrimazole	192004-01	1
Euro OTC	Clotrimazole	1703028-02	48
Euro OTC	Clotrimazole	1808028_01	1
Euro OTC	Clotrimazole	1105014-02	1
Euro OTC	Clotrimazole	1203040-02	8
Euro OTC	Clotrimazole	1210039-01	24
Euro OTC	Clotrimazole	12082013C	1
Euro OTC	Clotrimazole	121003901	3
Euro OTC	Clotrimazole	21122013A	1
Euro OTC	Clotrimazole	15042014C	1
Euro OTC	Clotrimazole	15072014A	1
Euro OTC	Clotrimazole	22122014B	1
Euro OTC	Clotrimazole	1309054-02	1
Euro OTC	Clotrimazole	21052015B	1
Euro OTC	Clotrimazole	1605003C	1
Euro OTC	Clotrimazole	16B11-B04-320088	1
Euro OTC	Clotrimazole	151000	1
Euro OTC	Clotrimazole	1607046-01	60
Euro OTC	Clotrimazole	170302801-01	1
Euro OTC	Clotrimazole	1808028_02	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Clotrimazole	1203040	1
Euro OTC	Clotrimazole	1808018-01	1
Euro OTC	Clotrimazole	1902004-02	3
Euro OTC	Clotrimazole	1828028-01	1
Euro OTC	Clotrimazole	151003-01	1
Euro OTC	Clotrimazole	110501402	1
Euro OTC	Clotrimazole	1409027-02Mg10g	1
Euro OTC	Clotrimazole	160704601	5
Euro OTC	Clotrimazole	41(1808028-01)	1
Euro OTC	Clotrimazole	1607046-0	1
Euro OTC	Clotrimazole	17A021	1
Euro OTC	Clotrimazole	1314Q1276	1
Euro OTC	Clotrimazole	16234511	1
Euro OTC	Clotrimazole	14C04-B31-291660	1
Euro OTC	Clotrimazole	140927-02	1
Euro OTC	Clotrimazole	170302803	1
Euro OTC	Clotrimazole	180802801	2
Euro OTC	Clotrimazole	180802802	1
Euro OTC	Clotrimazole	1902004-01	33
Euro OTC	Clotrimazole	190200401	1
Euro OTC	Clotrimazole	17111606	1
Euro OTC	Clotrimazole	1108053-01	1
Euro OTC	Clotrimazole	700135	2
Euro OTC	Clotrimazole	20130512	1
Euro OTC	Clotrimazole	1607046	1
Euro OTC	Clotrimazole	17053183	1
Euro OTC	Clotrimazole	17360201	1
Euro OTC	Clotrimazole	1409027	6
Euro OTC	Clotrimazole	140902702	3
Euro OTC	Clotrimazole	1703028-03	40
Euro OTC	Clotrimazole	160704602	1
euro//Noweda	Clotrimazole	1808028-01	1
EUro/AHD	Clotrimazole	1210039-01	2
Euro/Gehe	Clotrimazole	1607046-02	1
Euro/Gehe	Clotrimazole	1703028-03	1
Euro/Gehe	Clotrimazole	18A18-B05-350778	1
Euro/Noweda	Clotrimazole	1510003-02	1
Euro OTC	Clotrimazole	6051501	1
Euroo / Phönix	Clotrimazole	1409027-02	3
Euro OTC	Clotrimazole	1510003-01	53
Euro OTC	Clotrimazole	1409027-04	28
Euro OTC	Clotrimazole	1607064-01	1
Euro OTC	Clotrimazole	22091806	1
Euro OTC	Clotrimazole	1609046-01	1
Euro OTC	Clotrimazole	140927-01	1
Euro OTC	Clotrimazole	151000-01	1
Euro OTC	Clotrimazole	19016108	1
Euro OTC	Clotrimazole	1309034-02	20
Euro OTC	Clotrimazole	130636-01	2
Euro OTC	Clotrimazole	2214A-01276	1
Euro OTC	Clotrimazole	16234505	1
Euro OTC	Clotrimazole	1607046-02	30
Europ Ots Pharma	Clotrimazole	13184105	1
Euopharm/Otto	Clotrimazole	1203040-01	1
Euopharm/Otto	Clotrimazole	1203040-02	1
euopharma	Clotrimazole	1306036-01	1
EuroTOC / Noweda	Clotrimazole	1409027-03	1
Fagron	Clotrimazole	14B05-B35-294935	4
Fagron	Clotrimazole	11E17-N10	2
Fagron	Clotrimazole	20111018	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Clotrimazole	12I21N04	1
Fagron	Clotrimazole	12I21-N04	7
Fagron	Clotrimazole	20151112-3	1
Fagron	Clotrimazole	12/21-N04	3
Fagron	Clotrimazole	11G15-N10	1
Fagron	Clotrimazole	12I21-N04	2
Fagron	Clotrimazole	12F02-N12	1
Fagron	Clotrimazole	1221n04	1
Fagron	Clotrimazole	9041304	1
Fagron	Clotrimazole	1221N04	1
Fagron	Clotrimazole	6C16MU1	1
Fagron	Clotrimazole	13224201	1
Fagron	Clotrimazole	14C04-B30-291656	10
Fagron	Clotrimazole	1309034-01	3
Fagron	Clotrimazole	14C04-B30	1
Fagron	Clotrimazole	14B05-B36-291167	5
Fagron	Clotrimazole	14b05b36291166	1
Fagron	Clotrimazole	14223201	1
Fagron	Clotrimazole	14C04-B31-294939	6
Fagron	Clotrimazole	14B05-B35-293544	5
Fagron	Clotrimazole	14B05-B35-293542	3
Fagron	Clotrimazole	14b05-b36-291166	1
Fagron	Clotrimazole	14C04-B30-291661	3
Fagron	Clotrimazole	14B05-B36-291165	2
Fagron	Clotrimazole	14C04-B31-294951	1
Fagron	Clotrimazole	14B05-B35-294932	1
Fagron	Clotrimazole	14C04-B31-299954	7
Fagron	Clotrimazole	14C04-B31-299960	6
Fagron	Clotrimazole	14E26-B02	1
Fagron	Clotrimazole	14B06-B06-299942	1
Fagron	Clotrimazole	1409027-02	1
Fagron	Clotrimazole	14B06-B06-299943	6
Fagron	Clotrimazole	14b05-b35-299941	1
Fagron	Clotrimazole	14C04-B312-299959	1
Fagron	Clotrimazole	15g14-b06-311054	1
Fagron	Clotrimazole	15G14-B06-311056	2
Fagron	Clotrimazole	15G14B06311054	1
Fagron	Clotrimazole	14C04-B31-299955	1
Fagron	Clotrimazole	15G14-B05-311103	5
Fagron	Clotrimazole	16B09-B06-311507	5
Fagron	Clotrimazole	16B09-B06-311506	4
Fagron	Clotrimazole	CLT/1604/00227A	1
Fagron	Clotrimazole	15G14-B05-316483	1
Fagron	Clotrimazole	160704602	1
Fagron	Clotrimazole	16B11-B04-327611	3
Fagron	Clotrimazole	16B11-B04	1
Fagron	Clotrimazole	1703028-01	1
Fagron	Clotrimazole	17A19-B04_332114	1
Fagron	Clotrimazole	16J07-B02-330216	5
Fagron	Clotrimazole	17A19-B04332114	1
Fagron	Clotrimazole	16234521	1
Fagron	Clotrimazole	17A19-B04-338560	1
Fagron	Clotrimazole	17A19-B04-334768	1
Fagron	Clotrimazole	16J07_B02	1
Fagron	Clotrimazole	16J07-B02-340511	2
Fagron	Clotrimazole	17A19-B04-338577	2
Fagron	Clotrimazole	16J07-B02-344818	7
Fagron	Clotrimazole	16J07-B02-341842	1
Fagron	Clotrimazole	17J25-B06-345045	1
Fagron	Clotrimazole	17J25-B06-345407	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Clotrimazole	18A18-B05-347865	4
Fagron	Clotrimazole	16J07-B02-344817	3
Fagron	Clotrimazole	17J25-B06-347476	2
Fagron	Clotrimazole	17J25-B06-349161	2
Fagron	Clotrimazole	18a18-b05-348429	1
Fagron	Clotrimazole	700120-0003	1
Fagron	Clotrimazole	18A18-B05-350778	5
Fagron	Clotrimazole	18G10-B06-353348	2
Fagron	Clotrimazole	700135-0003	1
Fagron	Clotrimazole	18A18-B05-350781	1
Fagron	Clotrimazole	18G10-B06-352425	1
Fagron	Clotrimazole	18A18B05	1
Fagron	Clotrimazole	18147217	1
Fagron	Clotrimazole	16E20-B10-327349	5
Fagron	Clotrimazole	19B14-B01-359532	1
Fagron	Clotrimazole	CLT/1711/0077A	1
Fagron	Clotrimazole	19B14-B01-359537	1
Fagron	Clotrimazole	19B14-B01-361607	2
Fagron	Clotrimazole	18A18-B05-353892	3
Fagron	Clotrimazole	14B05-B35	2
Fagron	Clotrimazole	14C04-B32-291657	1
Fagron	Clotrimazole	14b05-b35-294935	1
Fagron	Clotrimazole	15G14-Bo5-311101	1
Fagron	Clotrimazole	1210039-01	1
Fagron	Clotrimazole	16E20-B10-324555	3
Fagron	Clotrimazole	CLT/1607/0060A	1
Fagron	Clotrimazole	18A18-B05-350780	4
Fagron	Clotrimazole	14B05-B35-299941	2
Fagron	Clotrimazole	19B14-B01-359531	1
Fagron	Clotrimazole	12B27-N05	3
Fagron	Clotrimazole	12721-N01	1
Fagron	Clotrimazole	12E30-N02	1
Fagron	Clotrimazole	11L12-N10	5
Fagron	Clotrimazole	12A05-N10	2
Fagron	Clotrimazole	17J25-B06-345044	2
Fagron	Clotrimazole	18A18-B05-355041	1
Fagron	Clotrimazole	11K21-N19	1
Fagron	Clotrimazole	12E02-N12	9
Fagron	Clotrimazole	18A18-B05-352114	2
Fagron	Clotrimazole	12I16-N04	1
Fagron	Clotrimazole	11A05-N14	2
Fagron	Clotrimazole	12/21-N01	5
Fagron	Clotrimazole	20171127Ma1	1
Fagron	Clotrimazole	16J07-B02-340513-201	1
Fagron	Clotrimazole	20170427Ma9	1
Fagron	Clotrimazole	14C04-B31-294940	1
Fagron	Clotrimazole	12K15-N01	1
Fagron	Clotrimazole	13C25-N10	9
Fagron	Clotrimazole	17A19-804-38560	2
Fagron	Clotrimazole	16J07-B02-333606	2
Fagron	Clotrimazole	14b05-b35-293544	1
Fagron	Clotrimazole	15G14-B06-31105	1
Fagron	Clotrimazole	19B14-B01-363547	1
Fagron	Clotrimazole	16J07-B02-338283	6
Fagron	Clotrimazole	3716Q-01276	1
Fagron	Clotrimazole	12a05-n10	1
Fagron	Clotrimazole	16E20-B10-326010	3
Fagron	Clotrimazole	16607-B02-333606	1
Fagron	Clotrimazole	16B09-B06	1
Fagron	Clotrimazole	12e02-N12	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Clotrimazole	16E20-B10-321598	9
Fagron	Clotrimazole	16E20-B10-32197	1
Fagron	Clotrimazole	CLT/160/00058	1
Fagron	Clotrimazole	CLT/150570016b	1
Fagron	Clotrimazole	14C04B32291657	1
Fagron	Clotrimazole	15G14-B06	1
Fagron	Clotrimazole	15G14-B05-311100	11
Fagron	Clotrimazole	C22H17CIN2	1
Fagron	Clotrimazole	4812E-01276(NP)	1
Fagron	Clotrimazole	14B05-B36-291168	2
Fagron	Clotrimazole	CLT/1307/0065A	2
Fagron	Clotrimazole	15G14-B05-311101	1
Fagron	Clotrimazole	18A18-B05-348429	3
Fagron	Clotrimazole	18a18-b05-352115	1
Fagron	Clotrimazole	14b05-B36-291167	1
Fagron	Clotrimazole	17A19-B04-340476	1
Fagron	Clotrimazole	18610_B06	1
Fagron	Clotrimazole	15G14-B06-311055	2
Fagron	Clotrimazole	16J07-B02-329385	3
Fagron	Clotrimazole	18G10-B06-352708	1
Fagron	Clotrimazole	16B09-B06-311785	2
Fagron	Clotrimazole	14B05-B36-291166	3
Fagron	Clotrimazole	14B05-B35-293543	1
Fagron	Clotrimazole	14B05-B36-2991166	1
Fagron	Clotrimazole	14B05-B35-299944	2
Fagron	Clotrimazole	16E20-B10-321597	2
Fagron	Clotrimazole	16J07-B02-329386	2
Fagron	Clotrimazole	16J07-B02-340513	4
Fagron	Clotrimazole	16J07B02347864	1
Fagron	Clotrimazole	18A18-B05-344819	1
Fagron	Clotrimazole	1A1-B05-34765	1
Fagron	Clotrimazole	18A18-B05-349662	1
Fagron	Clotrimazole	18A18B05353892	1
Fagron	Clotrimazole	14C04B31	1
Fagron	Clotrimazole	15G14-B05	4
Fagron	Clotrimazole	CLT/1604/0027A	2
Fagron	Clotrimazole	16J07-B02-337573	3
Fagron	Clotrimazole	17360201	1
Fagron	Clotrimazole	16J07-B02-344816	2
Fagron	Clotrimazole	16J07-B02-347864	4
Fagron	Clotrimazole	18G10-B06-352426	2
Fagron	Clotrimazole	19B14-B01	1
Fagron	Clotrimazole	2616A-01276	1
Fagron	Clotrimazole	14B05B35294935	1
Fagron	Clotrimazole	12E30-N07	11
Fagron	Clotrimazole	14337801	1
Fagron	Clotrimazole	14C04-B31-294952	1
Fagron	Clotrimazole	14B06-B06	1
Fagron	Clotrimazole	14337818	1
Fagron	Clotrimazole	1510003-01	1
Fagron	Clotrimazole	14337827	1
Fagron	Clotrimazole	17A19-SB04-332097	1
Fagron	Clotrimazole	17J25-B06	3
Fagron	Clotrimazole	14C04-B31-291660	4
Fagron	Clotrimazole	14B05B36291167	1
Fagron	Clotrimazole	18A18-B05-352115	2
Fargon	Clotrimazole	16234511	1
Fargon	Clotrimazole	17J25-B06-345406	1
Fargon/Phönix	Clotrimazole	18147103	1
Fargron / Noweda	Clotrimazole	16E20-B10-324555	1

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Supplier	Substance	Batch	Spectra
Fiebig	Clotrimazole	1607046-01	1
Fiebig	Clotrimazole	1607046-02	1
Fiebig	Clotrimazole	1703028	1
Fiebig	Clotrimazole	1703028-03	1
Fiebig	Clotrimazole	1808028-02	1
Fiebig 10.06.13 ek: 8,58EUR	Clotrimazole	12E30-N07	1
Finteler Apotheke	Clotrimazole	16234501	1
Finteler Apotheke	Clotrimazole	16234509	1
Fischar/Gehe	Clotrimazole	20111018	1
Fragron/noweda	Clotrimazole	CLT/1601/0005B	1
Fragron/noweda	Clotrimazole	17A19-B04	1
Gatt-Koller	Clotrimazole	201714s9	1
Gatt-Koller	Clotrimazole	1801870	1
Gehe	Clotrimazole	1108053-01	1
Gehe	Clotrimazole	12/21-N01	1
Gehe	Clotrimazole	11K21-N19	1
Gehe	Clotrimazole	13184103	1
Gehe	Clotrimazole	1306036-01	3
Gehe	Clotrimazole	121003902	1
Gehe	Clotrimazole	13224216	1
Gehe	Clotrimazole	1309034-01	1
Gehe	Clotrimazole	14C04-B31-294952	1
Gehe	Clotrimazole	14337815	2
Gehe	Clotrimazole	1409027-02	1
Gehe	Clotrimazole	15G14-B05	1
Gehe	Clotrimazole	16E20-B10-321598	1
Gehe	Clotrimazole	16234513	1
Gehe	Clotrimazole	17A19-B04	1
Gehe	Clotrimazole	1703028-02	1
Gehe	Clotrimazole	17J25-B06-0345044	1
Gehe	Clotrimazole	1808028-01	3
Gehe	Clotrimazole	1808028-02	1
Gehe	Clotrimazole	19016108	1
Gehe	Clotrimazole	HCZ14218	1
Gehe	Clotrimazole	1902004-02	1
GEHE	Clotrimazole	1607046-02	1
GEHE	Clotrimazole	16234513	1
GEHE	Clotrimazole	177111613	1
GEHE	Clotrimazole	16J07-B02	1
GEHE	Clotrimazole	18147103	1
GEHE	Clotrimazole	18147210	2
Caelo	Clotrimazole	130603601	1
Caelo	Clotrimazole	14144914	8
Euro OTC	Clotrimazole	120304002	1
Caelo	Clotrimazole	1070716	1
Caelo	Clotrimazole	170302801	2
Caelo	Clotrimazole	17111603	3
Caelo	Clotrimazole	1703028-02	1
Caelo	Clotrimazole	1814211	1
Caelo	Clotrimazole	10247328	3
Fagron	Clotrimazole	16B11-B04-320088	6
Caelo	Clotrimazole	14337814	8
Caelo	Clotrimazole	19016208	3
Guangzhou Hanpu Pharm./...	Clotrimazole	14337819	1
Guangzhou Hanpu Pharmac.	Clotrimazole	1703028-02	1
Guangzhou Hanpu Pharmac...	Clotrimazole	1409027-03	1
Guangzhou Hanpu Pharmac...	Clotrimazole	1510003-01	1
Guangzhou Hanpu Pharmac...	Clotrimazole	1510003-02	1
Halcyon Labs	Clotrimazole	19016104	1
Hedinger/Alliance H.	Clotrimazole	15395617	1

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Supplier	Substance	Batch	Spectra
Hedinger/Gehe	Clotrimazole	1703028-02	1
Henry Lamotte oils GmbH	Clotrimazole	18147203	1
Jenne	Clotrimazole	18147103	1
Caelo	Clotrimazole	19016104	6
Caelo	Clotrimazole	19016205	5
Caelo	Clotrimazole	14c04-b30-291656	1
Kehr	Clotrimazole	1808028-01	1
Klenk	Clotrimazole	16B09-B06-311785	1
Klosterring	Clotrimazole	6234505	1
Klosterring	Clotrimazole	16234512	1
Klosterring	Clotrimazole	17111615	2
L12	Clotrimazole	16234512	1
L12	Clotrimazole	17111606	1
L12	Clotrimazole	17360204	1
Martin Apo	Clotrimazole	31117/1	1
Midas	Clotrimazole	1703028-01	1
Midas	Clotrimazole	1703028-03	1
Midas	Clotrimazole	1808028-02	1
Mvda_15.01.2019	Clotrimazole	18147102	1
Noweda	Clotrimazole	1203040-03	2
Noweda	Clotrimazole	20111115	1
Noweda	Clotrimazole	13224201	1
Noweda	Clotrimazole	13224217	1
Noweda	Clotrimazole	1409027-02	1
Noweda	Clotrimazole	14337801	1
Noweda	Clotrimazole	1409027	1
Noweda	Clotrimazole	14337816	1
Noweda	Clotrimazole	1510003-01	2
Noweda	Clotrimazole	15G14-B05-316483	2
Noweda	Clotrimazole	16234511	1
Noweda	Clotrimazole	16J07-B02-329386	1
Noweda	Clotrimazole	16234517	2
Noweda	Clotrimazole	17111608	1
Noweda	Clotrimazole	18147203	1
Caelo	Clotrimazole	1409027-02	2
Noweda 06.11.2019	Clotrimazole	19016119	1
Noweda 07.07.2015	Clotrimazole	14144913	1
Noweda 17.7.2019	Clotrimazole	19016105	1
Bombastus	Clotrimazole	1607046-01	2
Euro OTC	Clotrimazole	170302802	1
Noweda/Apomix	Clotrimazole	15G14-B05-311100	1
Caelo	Clotrimazole	13224221	2
Euro OTC	Clotrimazole	14144914	1
Fagron	Clotrimazole	17A19-B04-336568	1
Fagron	Clotrimazole	18G10-B06352708	1
Noweda/Fagron	Clotrimazole	17A19-B04-336568	1
Oberlinden Apotheke	Clotrimazole	201401300378	2
Euro OTC	Clotrimazole	1203040-01	1
Euro OTC	Clotrimazole	1309034	1
Euro OTC	Clotrimazole	1409027_03	1
p&m cosmetics/gehe	Clotrimazole	16J07-B02-335773	2
Caelo	Clotrimazole	19015107	1
phoenix	Clotrimazole	16234512	1
Phoenix	Clotrimazole	12A05-N10	1
Phoenix	Clotrimazole	13224215	1
Phoenix	Clotrimazole	1309034-02	1
Phoenix	Clotrimazole	14c04b31	1
Phoenix	Clotrimazole	14337812	1
Phoenix	Clotrimazole	1607046-01	1
Phoenix	Clotrimazole	79879	1

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Supplier	Substance	Batch	Spectra
Phoenix	Clotrimazole	3088	1
Phoenix	Clotrimazole	17111601	1
Phoenix	Clotrimazole	3237	1
Phoenix	Clotrimazole	18147102	1
Phoenix	Clotrimazole	16B11-B04-327611	1
Phoenix	Clotrimazole	1902004-01	1
Euro OTC	Clotrimazole	1203040-03	9
Phoenix 23.10.14 5,50	Clotrimazole	1309034-02	1
PHÖNIX am 22.01.2014	Clotrimazole	1306036-01	1
phönix	Clotrimazole	11305513	1
phönix	Clotrimazole	14337818	1
phönix	Clotrimazole	16B11-B04-327611	1
phönix	Clotrimazole	16234512	1
Phönix	Clotrimazole	13C25-N10	1
Phönix	Clotrimazole	16234505	1
Phönix	Clotrimazole	15395618	1
Phönix	Clotrimazole	18G10-B06-354620	2
Phönix	Clotrimazole	1902004-01	1
Phönix	Clotrimazole	1902004-02	1
PHÖNIX	Clotrimazole	18147203	1
Caelo	Clotrimazole	16234525	3
Phönix Gotha	Clotrimazole	14337811	1
Phönix WE:23.10.17 EK:...	Clotrimazole	16234521	1
Caelo	Clotrimazole	16J07-B02-335773	1
sanacorp	Clotrimazole	14144918	1
Sanacorp	Clotrimazole	12159902	1
Sanacorp	Clotrimazole	1203040-03	1
Sanacorp	Clotrimazole	12320814	1
Sanacorp	Clotrimazole	1230805	1
Sanacorp	Clotrimazole	13184105	1
Sanacorp	Clotrimazole	13224214	2
Sanacorp	Clotrimazole	105/AKD1	1
Sanacorp	Clotrimazole	14144905	1
Sanacorp	Clotrimazole	13224219	1
Sanacorp	Clotrimazole	109/AKD3	1
Sanacorp	Clotrimazole	109/AKD6	1
Sanacorp	Clotrimazole	14337817	1
Sanacorp	Clotrimazole	16E20-B10-327349	1
Sanacorp	Clotrimazole	15g14-b05-311100	1
Sanacorp	Clotrimazole	16J07-B02-330216	1
Sanacorp	Clotrimazole	16J07-B02-338283	1
Sanacorp	Clotrimazole	17360203	1
Sanacorp	Clotrimazole	17360201	1
Sanacorp	Clotrimazole	18147102	1
Sanacorp	Clotrimazole	18147212	1
Caelo	Clotrimazole	1105014-02	1
Caelo	Clotrimazole	11/22-N10	1
Sanacorp/Caela	Clotrimazole	17111603	1
Caelo	Clotrimazole	11305506	2
Caelo	Clotrimazole	13148007	1
Caelo	Clotrimazole	108/AKD1	1
Fagron	Clotrimazole	16J07-B02	1
Sino Phyto	Clotrimazole	13224210	2
Stumpf	Clotrimazole	12159902	1
Caelo	Clotrimazole	12320805	4
Vdl 14.07.14	Clotrimazole	13224225	1
Caelo	Clotrimazole	11305513	8
VDL;11.06.15;27,90EUR	Clotrimazole	14337807	1
WE Phönix.01.12.2016 ...	Clotrimazole	15395618	1
wepa/Sanaco	Clotrimazole	14337819	1

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Supplier	Substance	Batch	Spectra
	Clotrimazole	1306036-01	1
Caelo	Clotrimazole		9
Caelo	Clotrimazole	13184113	2
Caelo	Clotrimazole	13224220	6
Euro OTC	Clotrimazole	1306036-01	39
Euro OTC	Clotrimazole		4
Fagron	Clotrimazole	12I21-N01	7
Fagron	Clotrimazole		2
Fagron	Clotrimazole	14C04-B31	8
Fagron	Clotrimazole	14B05-B36	7
Caelo	Clotrimazole	13224204	2
	Clotrimazole	14C04-B30-291661	1

- 108 362 spectra from 742 *Apo-Ident* customers from a total of 31 368 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Clotrimazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clotrimazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	420	0	110 269
Type B	0	350	0	118 792
Type C	0	2863	22	108 362

The substance/substance group *Clotrimazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5714 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.2857 %)
Type C	100.0000 % (> 99.8899 %)	99.2374 % (> 99.1334 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Clotrimazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bifonazole	19.90	—
Ciprofloxacin hydrochloride	46.33	—
Midazolam hydrochloride	48.70	—
Methoxsalen	61.74	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Clotrimazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20794	22229	3.47	36.96
21087	23791	2.97	35.31
21114	23791	2.98	34.31
21207	22229	6.19	33.38
21259	22229	6.67	36.52
21264	22229	4.75	33.55
21352	22229	4.25	33.83
21353	22229	4.38	33.31
22229	22229	0.00	35.20
23791	23791	0.00	34.59

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Colistin sulfate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20318-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Colistin sulfate; Colistin sulphate; Colistini sulfas

Special notes

When selecting the *Colistin sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Colistin sulfate	9	6	7

Second-stage model

For differentiation of the substance/substance group *Colistin sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Colistin sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Colistin sulfate	APKB-CS-1602026C	22974	40	20160418
Audor Pharma	Colistin sulfate	APKB-CS-1603034C	23026	40	20160627
Audor Pharma	Colistin sulfate	APKB-CS-1602026C	23027	40	20160418
Euro OTC	Colistin sulfate	1406001-01	21619	60	1508600
Euro OTC	Colistin sulfate	1507044	21852	60	20150817*
Euro OTC	Colistin sulfate	1602021	22371	60	20160307*
Euro OTC	Colistin sulfate	1606008	22695	40	20160704*
Fagron	Colistin sulfate	13G05-N01	20915	40	20130719
Fagron	Colistin sulfate	13G05-N01	21209	40	20130719
Fagron	Colistin sulfate	14E02-B03	21346	40	1501654
Fagron	Colistin sulfate	16F03-B01-324216	22973	40	20160706

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 11 reference samples from the substance/substance group *Colistin sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 189 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 245 spectra of 6 reference samples from the substance/substance group *Colistin sulfate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Colistin sulfate	1406002-01	21700	45
Euro OTC	Colistin sulfate	1709009	23616	40
Euro OTC	Colistin sulfate	1710041	23866	40
Euro OTC	Colistin sulfate	1905016	24769	40
Euro OTC	Colistin sulfate	1908007	24836	40
Euro OTC	Colistin sulfate	2001039	25087	40

- 118 897 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 10 spectra from 4 *Apo-Ident* customers from 9 batches from the substance/substance group *Colistin sulfate*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Colistin sulfate	APKB-CS-1601026C	1
Audor Pharma	Colistin sulfate	APKB-CS-1610012C	1
Caelo	Colistin sulfate	1602021-01	1
Euro OTC	Colistin sulfate	1507044-01	1
Fagron	Colistin sulfate	15E15-B01-315340	1
Fagron	Colistin sulfate	16F03-B01	1
Fagron	Colistin sulfate	17E09-B04-342085	1
Audor Pharma	Colistin sulfate	APKB-CS-1603034C	2
Fagron	Colistin sulfate	16F03-B01-324216	1

- 111 237 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Colistin sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Colistin sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following

table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	500	0	110 189
Type B	0	245	0	118 897
Type C	0	10	0	111 237

The substance/substance group *Colistin sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5510 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Colistin sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Nystatin	20.03	—
Bacitracin	22.67	—
Citrulline	23.12	—
Calcium pantothenate	23.39	—
Estradiol hemihydrate	24.54	—
Polymyxin B sulfate	26.01	—
Thiamine chloride hydrochloride	27.44	—
Magnesium citrate	33.99	—
Clindamycin hydrochloride	36.17	—
Amphotericin B	41.40	—
Calcium citrate tetrahydrate	48.12	—
Minoxidil	50.32	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Colistin sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22371	22371	0.00	26.83
22695	22695	0.00	27.57
23026	21346	12.52	22.67
20915	22371	2.39	27.28
21209	21619	3.08	26.44
21619	21619	0.00	26.71
21852	21852	0.00	25.21
22973	21852	1.32	24.94
21346	21346	0.00	22.84
22974	21852	7.46	23.90
23027	21346	8.74	23.45

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Cyanocobalamin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 10003566-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cyanocobalamin; Cyanocobalaminum

Special notes

When selecting the *Cyanocobalamin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cyanocobalamin	7	4	13

Second-stage model

For differentiation of the substance/substance group *Cyanocobalamin* the following second-stage model is used:

- [Submodel 4](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cyanocobalamin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Cyanocobalamin	13342803	21299	40	AR-15-FG-005429-01
Caelo	Cyanocobalamin	13342807	21479	60	AR-15-FG-014917-01
Caelo	Cyanocobalamin	13342807	21479SI	30	AR-15-FG-014917-01
Caelo	Cyanocobalamin	160154	22441	60	20160309*
Caelo	Cyanocobalamin	160154	22441SI	60	20160309*
Euro OTC	Cyanocobalamin	1305040-01	21635	60	AR-15-FG-005214-01
Euro OTC	Cyanocobalamin	1506035	21867	60	20150708*
Euro OTC	Cyanocobalamin	1506035	21867SI	60	20150708*
Euro OTC	Cyanocobalamin	1506035	21872	60	0000010479
Euro OTC	Cyanocobalamin	1506035	21872SI	45	0000010479
Euro OTC	Cyanocobalamin	1604017	22536	30	20160509*
Euro OTC	Cyanocobalamin	1604017	22536SI	30	20160509*
Euro OTC	Cyanocobalamin	1812011	24465	40	20190205*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 635 spectra of 13 reference samples from the substance/substance group *Cyanocobalamin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 054 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 7 reference samples from the substance/substance group *Cyanocobalamin*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Cyanocobalamin	09351704	20858	40
Caelo	Cyanocobalamin	16015411	23761	40
Caelo	Cyanocobalamin	162215	23790	40
Euro OTC	Cyanocobalamin	1907030	24965	40
Caelo	Cyanocobalamin	13342807	21479SI [†]	30
Euro OTC	Cyanocobalamin	1604017	22536SI [†]	10
Euro OTC	Cyanocobalamin	1907030	24965SI	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 16 spectra from 12 *Apo-Ident* customers from 13 batches from the substance/substance group *Cyanocobalamin*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Cyanocobalamin	9324113	1
Caelo	Cyanocobalamin	9373503	2
Caelo	Cyanocobalamin	9351704	1
Caelo	Cyanocobalamin	16015405	1
Caelo	Cyanocobalamin	1604017-01	1
Caelo	Cyanocobalamin	9324102	1
Caesar & Loretz GmbH, 4...	Cyanocobalamin	9324102	1
Euro OTC	Cyanocobalamin	5061204	1
Fagron	Cyanocobalamin	10K02-N05	1
Fagron	Cyanocobalamin	10K02-N05	2
Fagron	Cyanocobalamin	17A27-B04	1
Fagron	Cyanocobalamin	13124-B01-292062	1
Fagron	Cyanocobalamin	17A27-B04-339672	1
Fagron	Cyanocobalamin	15H31-B02-315113	1

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- 111 231 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cyanocobalamin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cyanocobalamin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	635	0	110 054
Type B	0	240	0	118 902
Type C	0	16	0	111 231

The substance/substance group *Cyanocobalamin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0551 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cyanocobalamin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	14.77	29.38
Methylcobalamin	19.26	15.57
Ethinylestradiol	27.30	221.41
Magnesium citrate	32.40	—
Prednisone	34.60	—
Calcium citrate tetrahydrate	34.70	85.35
Minoxidil	37.97	—
Methylprednisolone	38.61	—
Gelatine, white	45.27	—
Levothyroxin sodium	45.32	—
Polymyxin B sulfate	48.47	—
Triamcinolone, micronized	49.05	—
Prednisolon dihydrogen phosphate dinat...	50.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cyanocobalamin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21299	21299	0.00	16.60
22441	22441	0.00	26.02
22536	22536	0.00	19.26
21635	21635	0.00	16.67
21867	21867	0.00	14.77
21872	21872	0.00	19.37
24465	24465	0.00	21.85
21479	21479	0.00	16.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Cyproterone acetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20593-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cyproterone acetate; Cyproteroni acetat

Special notes

When selecting the *Cyproterone acetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cyproterone acetate	8	3	34

Second-stage model

For differentiation of the substance/substance group *Cyproterone acetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cyproterone acetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Cyproterone acet...	APCPA140201CP	23988	40	20140617
Audor Pharma	Cyproterone acet...	APX03-181002-m0C	24814	40	20181213
Euro OTC	Cyproterone acet...	1611003	22875	40	20161201*
Euro OTC	Cyproterone acet...	1810017	24317	40	20181108*
Fagron	Cyproterone acet...	13C11-N02	21262	40	1501534
Fagron	Cyproterone acet...	13J16-No4	21985	75	1602654
Fagron	Cyproterone acet...	15I11-B01-322117	22665	40	20150921
Fagron	Cyproterone acet...	17D11-B07-333693	23238	40	20170501
Fagron	Cyproterone acet...	17D11-B07-333693	23238SI	20	20170501

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 375 spectra of 9 reference samples from the substance/substance group *Cyproterone acetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 314 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 348 spectra of 12 reference samples from the substance/substance group *Cyproterone acetate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Cyproterone acetate	1903011	24609	40
Euro OTC	Cyproterone acetate	1910022	24957	40
Fagron	Cyproterone acetate	18G25-B02-352728	24289	40
Audor Pharma	Cyproterone acetate	APCPA140201CP	23988SI [†]	20
Audor Pharma	Cyproterone acetate	APX03-181002-m0C	24814SI [†]	40
Euro OTC	Cyproterone acetate	1611003	22875SI [†]	30
Euro OTC	Cyproterone acetate	1810017	24317SI [†]	20
Euro OTC	Cyproterone acetate	1903011	24609SI	20
Euro OTC	Cyproterone acetate	1910022	24957SI	22
Fagron	Cyproterone acetate	13J16-No4	21985SI [†]	23
Fagron	Cyproterone acetate	15I11-B01-322117	22665SI [†]	33
Fagron	Cyproterone acetate	18G25-B02-352728	24289SI	20

- 118 794 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 50 spectra from 33 *Apo-Ident* customers from 36 batches from the substance/substance group *Cyproterone acetate*.
- Among them are spectra of independent samples from 34 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Cyproterone acetate	cpa140201cp	1
Audor Pharma	Cyproterone acetate	X03-181002-m0C	1
Caelo	Cyproterone acetate	13j16-n04	1
Caelo	Cyproterone acetate	17D11-B07-334581	3
Caelo	Cyproterone acetate	CPA150301	1
Ebert-Jacobi	Cyproterone acetate	16K09-B04-329036	1
Fagron	Cyproterone acetate	12F25-N09	3
Fagron	Cyproterone acetate	12D02-N13	1
Fagron	Cyproterone acetate	12L19-N05	3
Fagron	Cyproterone acetate	13/09-N03	1
Fagron	Cyproterone acetate	13J16-N04	2
Fagron	Cyproterone acetate	13j16n04	1
Fagron	Cyproterone acetate	13j16-no4	1
Fagron	Cyproterone acetate	15I11-B01-315381	2
Fagron	Cyproterone acetate	16K09-B04-329037	1
Fagron	Cyproterone acetate	EU-CPA-170301	1
Fagron	Cyproterone acetate	17D11-B07-338440	1

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Cyproterone acetate	18041805	1
Fagron	Cyproterone acetate	17D11-B07-336729	2
Fagron	Cyproterone acetate	17D11-B07	1
Fagron	Cyproterone acetate	20101807	1
Fagron	Cyproterone acetate	18G25-B02-352728	3
Fagron	Cyproterone acetate	18G25-B02-355388	1
Fagron	Cyproterone acetate	8B11-N06	1
Fagron	Cyproterone acetate	18G25-B02-354474	1
Fagron	Cyproterone acetate	18G25-B02-354476	1
Fagron	Cyproterone acetate	18B05-B05-346309	1
Fagron	Cyproterone acetate	B0392/110020	3
Fagron	Cyproterone acetate	13/16-N04	2
Fagron	Cyproterone acetate	18G25-B02-352307	1
Fagron	Cyproterone acetate	18B05_B05_346309	1
Fagron	Cyproterone acetate	12J24-N02	1
Fagron	Cyproterone acetate	15H04-B06-311064	1
Sanacorp	Cyproterone acetate	18B05-B05-346307	1
Fagron	Cyproterone acetate	11L22-N02	1
Audor Pharma	Cyproterone acetate	APCPA140201CP	1

- 111 197 spectra from 742 *Apo-Ident* customers from a total of 31 855 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cyproterone acetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cyproterone acetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	375	0	110 314
Type B	0	318	30	118 794
Type C	0	43	7	111 197

The substance/substance group *Cyproterone acetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.4000 %)
Type B	100.0000 % (> 99.9893 %)	91.3793 % (> 90.5172 %)
Type C	100.0000 % (> 99.8899 %)	86.0000 % (> 80.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cyproterone acetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prilocaine hydrochloride	30.05	—
Omeprazole	34.90	—
Atropine sulfate	44.77	—
Griseofulvin	55.25	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cyproterone acetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22875	22875	0.00	35.58
23238	24317	1.68	39.70
21262	21262	0.00	35.05
23988	21985	1.89	40.06
24317	24317	0.00	40.31
24814	21985	2.55	40.97
21985	21985	0.00	42.38
22665	21985	2.21	47.29

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Cystine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20515-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Cystine; Cystinum

Special notes

When selecting the *Cystine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cystine	6	3	8

Second-stage model

For differentiation of the substance/substance group *Cystine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Cystine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Cystine	1307052-01	21328	40	20130918
Euro OTC	Cystine	1408016-01	21715	60	20140911
Euro OTC	Cystine	1603010	22523	40	20160406*
Euro OTC	Cystine	1610013	22863	40	20161110*
Euro OTC	Cystine	1801016	23879	40	20180126*
Fagron	Cystine	15F08-B05-310685	23767	40	20150616

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Cystine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Cystine*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Cystine	1811005	24332	40
Euro OTC	Cystine	1904022	24617	40
Euro OTC	Cystine	1910028	24933	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 5 *Apo-Ident* customers from 9 batches from the substance/substance group *Cystine*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Cystine	2081301	1
Euro OTC	Cystine	26081408	1
Euro OTC	Cystine	3021502	1
Euro OTC	Cystine	30041809	1
Euro OTC	Cystine	1801016-01	2
Euro OTC	Cystine	1207013-01	2
Euro OTC	Cystine	1204090	1
Fagron	Cystine	12D26-B04-285823	2
Fagron	Cystine	15F08-B05-310685	1

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Cystine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cystine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	12	0	111 235

The substance/substance group *Cystine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cystine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lysine hydrochloride	38.65	—
Glycine	67.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Cystine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21328	22523	3.20	49.39
21715	22523	3.38	48.00
22523	22523	0.00	49.73
22863	22863	0.00	50.79
23767	23879	5.65	49.97
23879	23879	0.00	51.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Dapsone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22489-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dapsone; Dapsonum

Special notes

When selecting the *Dapsone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dapsone	3	2	1

Second-stage model

For differentiation of the substance/substance group *Dapsone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dapsone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dapsone	160735	22489	60	20160405*
Caelo	Dapsone	170311	23301	39	20170221*
Caelo	Dapsone	191135	24727	40	20190726*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 139 spectra of 3 reference samples from the substance/substance group *Dapsone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 550 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Dapsone*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Dapsone	16073502	22577	40
Caelo	Dapsone	182792	24400	40
Caelo	Dapsone	16073502	22736	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Dapsone*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Dapsone	19113501	1

- 111 246 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dapsone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dapsone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	139	0	110 550
Type B	0	120	0	119 022
Type C	0	1	0	111 246

The substance/substance group *Dapsone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.6835 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8911 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dapsone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sulfadiazine	55.68	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dapsone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22489	22489	0.00	55.68
23301	23301	0.00	61.07
24727	24727	0.00	63.98

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Dequalinium chloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20350-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dequalinium chloride; Dequalinii chloridum

Special notes

When selecting the *Dequalinium chloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dequalinium chloride	10	4	73

Second-stage model

For differentiation of the substance/substance group *Dequalinium chloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dequalinium chloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dequalinium chlo...	12361908	21296	40	1412076
Caelo	Dequalinium chlo...	12361906	21387	60	20121228
Caelo	Dequalinium chlo...	15218406	22953	40	20150622
Caelo	Dequalinium chlo...	15402803	23121	40	1707614
Caelo	Dequalinium chlo...	154028	23362	40	20160219*
Caelo	Dequalinium chlo...	154028	24403	40	20160219*
Euro OTC	Dequalinium chlo...	1405012-01	21617	60	20140623
Euro OTC	Dequalinium chlo...	1512032	22295	60	20160121*
Euro OTC	Dequalinium chlo...	1512032-02	24142	40	1809202
Fagron	Dequalinium chlo...	13I26-N10	21269	40	20130121
Fagron	Dequalinium chlo...	15B16-B04-332113	23266	40	20150226

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 11 reference samples from the substance/substance group *Dequalinium chloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 189 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 680 spectra of 13 reference samples from the substance/substance group *Dequalinium chloride*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Dequalinium chloride	12077503	20716	40
Caelo	Dequalinium chloride	180794	24011	40
Euro OTC	Dequalinium chloride	1804009	24082	40
Fagron	Dequalinium chloride	11D29-N11	20660	80
Caelo	Dequalinium chloride	12361906	21386	60
Caelo	Dequalinium chloride	12361906	21386SI	60
Caelo	Dequalinium chloride	12361906	21387 [†]	60
Caelo	Dequalinium chloride	12361906	21387SI [†]	60
Caelo	Dequalinium chloride	15218406	22953SI [†]	40
Caelo	Dequalinium chloride	154028	23362SI [†]	40
Euro OTC	Dequalinium chloride	1405012-01	21617SI [†]	60
Euro OTC	Dequalinium chloride	1512032	22295SI [†]	60
Fagron	Dequalinium chloride	15B16-B04-332113	23266SI [†]	40

- 118462 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 207 spectra from 146 *Apo-Ident* customers from 81 batches from the substance/substance group *Dequalinium chloride*.
- Among them are spectra of independent samples from 72 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Dequalinium chloride	15218401	1
Alliance Health	Dequalinium chloride	12077508	1
Allianz Healthcare	Dequalinium chloride	1512032-01	1
Anzag	Dequalinium chloride	15B16-B04-340177	1
Anzag ek:7.89EUR	Dequalinium chloride	11166204	1
Euro OTC	Dequalinium chloride	1407029-02	5
Caelo	Dequalinium chloride	11166203	1
Caelo	Dequalinium chloride	12G05-N07	1
Caelo	Dequalinium chloride	12077510	7
Caelo	Dequalinium chloride	220812K2	1
Caelo	Dequalinium chloride	12361911	3
Caelo	Dequalinium chloride	13A23-N02	1
Caelo	Dequalinium chloride	15218401	7
Caelo	Dequalinium chloride	15218404	2

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Dequalinium chloride	15402801	3
Caelo	Dequalinium chloride	15B16-B04-326872	1
Caelo	Dequalinium chloride	18015802	1
Caelo	Dequalinium chloride	15402807	2
Caelo	Dequalinium chloride	18079402	1
Caelo	Dequalinium chloride	10879409	1
Caelo	Dequalinium chloride	15B16-B04-342302	1
Caelo	Dequalinium chloride	152184	1
Caelo	Dequalinium chloride	11166204	2
Caelo	Dequalinium chloride	1405012-02	1
Caelo	Dequalinium chloride	11166209	1
Caelo	Dequalinium chloride	3613A-01325	1
Caelo	Dequalinium chloride	215I-01325	1
Caelo	Dequalinium chloride	15218410	1
Caelo	Dequalinium chloride	5315I-01325	1
Caelo	Dequalinium chloride	18015801	1
Caelo	Dequalinium chloride	12077508	2
Caelo	Dequalinium chloride	13/26-N10	1
Caelo	Dequalinium chloride	15B16-B04-337594	1
Caelo	Dequalinium chloride	18079407	1
Caelo	Dequalinium chloride	15402805	2
Caelo	Dequalinium chloride	18079404	1
Caelo	Dequalinium chloride	1512032-02	2
Caelo	Dequalinium chloride	19131402	2
Caelo	Dequalinium chloride	14C10-B03	1
Caelo	Dequalinium chloride	13348805	2
Caelo	Dequalinium chloride	18079403	3
Caesar & Loretz GmbH / ...	Dequalinium chloride	18079411	1
EuRho	Dequalinium chloride	1110002-01	1
EuRho/ Anzag	Dequalinium chloride	80(1804009-01)	1
Euro OTC	Dequalinium chloride	1512032-01	18
Euro OTC	Dequalinium chloride	15061204	1
Euro OTC	Dequalinium chloride	1210008-01	1
Euro OTC	Dequalinium chloride	1804009-01	5
Euro OTC	Dequalinium chloride	1210008-03	2
Euro OTC	Dequalinium chloride	1103045-01	1
Euro OTC	Dequalinium chloride	1110002-01	2
Euro OTC	Dequalinium chloride	1210008-02	2
Euro OTC	Dequalinium chloride	11091701	1
Euro OTC	Dequalinium chloride	81(1804009-01)	1
Euro/Sanacorp	Dequalinium chloride	1512032-02	1
Euro/Spangro	Dequalinium chloride	1512032-02	1
Euro OTC	Dequalinium chloride	1010022-01	2
Euro OTC	Dequalinium chloride	1407029-01	7
Euro OTC	Dequalinium chloride	1405012-02	6
Fag / Noweda	Dequalinium chloride	15B16-B04-321326	1
Fagron	Dequalinium chloride	12G05-N07	2
Fagron	Dequalinium chloride	12D05-N09	1
Fagron	Dequalinium chloride	13A23-N02	3
Fagron	Dequalinium chloride	14C10-B03	1
Fagron	Dequalinium chloride	12B14-N01	1
Fagron	Dequalinium chloride	15B16-B04-346969	3
Fagron	Dequalinium chloride	15B16-B04-354618	1
Fagron	Dequalinium chloride	10H05-N07	1
Fagron	Dequalinium chloride	15B16-B04-340177	1
Fagron	Dequalinium chloride	15B16-B04-304432	1
Fagron	Dequalinium chloride	15B16-B04-342302	2
Fagron	Dequalinium chloride	14C10-B03-292286	3
Fagron	Dequalinium chloride	15B16-B04-316267	2
Fagron	Dequalinium chloride	13D26-N06	3

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Supplier	Substance	Batch	Spectra
Fagron	Dequalinium chloride	14C10B03292286	1
Fagron	Dequalinium chloride	15B16-B04	1
Fagron	Dequalinium chloride	15B16-B04-326872	2
Gatt-Koller	Dequalinium chloride	1800212	1
Gehe	Dequalinium chloride	1512032-01	1
GEHE	Dequalinium chloride	1804009-01	1
Caelo	Dequalinium chloride	14072901	1
Euro OTC	Dequalinium chloride	151203201	1
Fagron	Dequalinium chloride	15B16B04304432	1
Th. Geyer	Dequalinium chloride	15B16-B04-354618	1
Klostering	Dequalinium chloride	15B16-B04-321326	1
L30	Dequalinium chloride	1804009-01	1
Lamotte/Spangroh	Dequalinium chloride	15218404	1
Lebsa/AHD	Dequalinium chloride	1405012-01	1
LEBSA/Phoenix	Dequalinium chloride	1210008-03	1
Noweda	Dequalinium chloride	12b14-n05	1
Caelo	Dequalinium chloride	15218402	1
Caelo	Dequalinium chloride	15218407	1
Phönix	Dequalinium chloride	10127-N02Retest	1
Phönix	Dequalinium chloride	151203201	1
Phönix	Dequalinium chloride	1110002-01	1
Raben-Apotheke Mildenau	Dequalinium chloride	1405012-01	1
S.Binder	Dequalinium chloride	1210008-04	1
Caelo	Dequalinium chloride	1210008-03	1
Fagron	Dequalinium chloride	1407029-01	2
Wepa Apothekenbedarf	Dequalinium chloride	151203202	1
Caelo	Dequalinium chloride		1
Caelo	Dequalinium chloride	15218406	6
Caelo	Dequalinium chloride	15402803	3
Caelo	Dequalinium chloride	12361908	2
Caelo	Dequalinium chloride	12361906	3
Euro OTC	Dequalinium chloride	1405012-01	5
Euro OTC	Dequalinium chloride	1512032-02	5
Fagron	Dequalinium chloride	13I26-N10	1
Fagron	Dequalinium chloride		2

- 111 040 spectra from 742 *Apo-Ident* customers from a total of 31 810 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dequalinium chloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dequalinium chloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	500	0	110 189
Type B	0	599	81	118 462
Type C	0	159	48	111 040

The substance/substance group *Dequalinium chloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.9893 %)	88.0882 % (> 87.6471 %)
Type C	100.0000 % (> 99.8899 %)	76.8116 % (> 75.3623 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dequalinium chloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	39.55	—
Serine	44.92	—
Choline hydrogen tartrate	54.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dequalinium chloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24142	24142	0.00	64.59
21296	21296	0.00	65.91
21617	21296	12.68	68.78
21269	21296	20.73	74.66
21387	21296	8.69	73.03
22953	21296	18.77	73.86
24403	24403	0.00	67.44
22295	22295	0.00	61.33
23121	23121	0.00	51.07
23266	22295	8.56	58.91
23362	23362	0.00	61.38

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Dexamethasone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20009-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dexamethasone; Dexamethasonum

Special notes

When selecting the *Dexamethasone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dexamethasone	8	10	223

Second-stage model

For differentiation of the substance/substance group *Dexamethasone* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dexamethasone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dexamethasone	13084315	21403	60	AR-15-FG-006810-01
Caelo	Dexamethasone	15054627	23169	40	20150420
Caelo	Dexamethasone	190221	24504	40	20190214*
Caelo	Dexamethasone	190221	24504SI	40	20190214*
Euro OTC	Dexamethasone	1303007-01	21289	40	1407432
Euro OTC	Dexamethasone	1303007-01	21850	60	20130328
Euro OTC	Dexamethasone	1601052	22364	45	20160225*
Euro OTC	Dexamethasone	1601052	22364SI	45	20160225*
Euro OTC	Dexamethasone	1611001	22914	40	20161212*
Euro OTC	Dexamethasone	1611001	22914SI	37	20161212*
Fagron	Dexamethasone	16F02-B05-324844	23168	40	20160711
Fagron	Dexamethasone	19A24-B01-361445	24705	40	20190403

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 527 spectra of 12 reference samples from the substance/substance group *Dexamethasone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 162 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 858 spectra of 22 reference samples from the substance/substance group *Dexamethasone*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Dexamethasone	13084306	21062	60
Caelo	Dexamethasone	171042	23331	40
Caelo	Dexamethasone	172856	23841	40
Caelo	Dexamethasone	190865	24742	40
Euro OTC	Dexamethasone	1209008-02	21078	60
Euro OTC	Dexamethasone	1708004	23692	40
Euro OTC	Dexamethasone	1806023	24136	40
Euro OTC	Dexamethasone	1909011	24839	40
Euro OTC	Dexamethasone	1708004-02	24867	40
Fagron	Dexamethasone	19A24-B01-359626	24573	40
Caelo	Dexamethasone	15054627	23169SI [†]	20
Caelo	Dexamethasone	171042	23331SI	24
Caelo	Dexamethasone	172856	23841SI	40
Caelo	Dexamethasone	190865	24742SI	40
Euro OTC	Dexamethasone	1303007-01	21850SI [†]	45
Euro OTC	Dexamethasone	1708004	23692SI	26
Euro OTC	Dexamethasone	1806023	24136SI	33
Euro OTC	Dexamethasone	1909011	24839SI	40
Euro OTC	Dexamethasone	1708004-02	24867SI	40
Fagron	Dexamethasone	16F02-B05-324844	23168SI [†]	30
Fagron	Dexamethasone	19A24-B01-359626	24573SI	40
Fagron	Dexamethasone	19A24-B01-361445	24705SI [†]	40

- 118284 spectra from a total of 2406 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1157 spectra from 424 *Apo-Ident* customers from 233 batches from the substance/substance group *Dexamethasone*.
- Among them are spectra of independent samples from 223 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Dexamethasone	17L19-B03-344099	1
AHD	Dexamethasone	1806023-01	1
ALH	Dexamethasone	15054617	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Alliance/Caeolo	Dexamethasone	19086503	1
Anzag	Dexamethasone	1233305	1
Anzag	Dexamethasone	17332404	1
Caelo	Dexamethasone	1708804-01	1
Bombastus	Dexamethasone	150546629	1
Bombastus	Dexamethasone	17332418	1
Caelo	Dexamethasone	10369921	2
Caelo	Dexamethasone	12033305	4
Caelo	Dexamethasone	9383631	1
Caelo	Dexamethasone	12033308	2
Caelo	Dexamethasone	12165803	1
Caelo	Dexamethasone	12033304	1
Caelo	Dexamethasone	12033315	4
Caelo	Dexamethasone	12091306	1
Caelo	Dexamethasone	3084310	1
Caelo	Dexamethasone	13084307	2
Caelo	Dexamethasone	13084309	1
Caelo	Dexamethasone	13084313	2
Caelo	Dexamethasone	13084316	3
Caelo	Dexamethasone	13084317	6
Caelo	Dexamethasone	13352302	9
Caelo	Dexamethasone	13084319	4
Caelo	Dexamethasone	1203304788	1
Caelo	Dexamethasone	13352312	13
Caelo	Dexamethasone	15054602	6
Caelo	Dexamethasone	13342310	1
Caelo	Dexamethasone	15054605	7
Caelo	Dexamethasone	15054609	5
Caelo	Dexamethasone	15054614	4
Caelo	Dexamethasone	160821D	1
Caelo	Dexamethasone	15054616	4
Caelo	Dexamethasone	2884	1
Caelo	Dexamethasone	15054623	7
Caelo	Dexamethasone	15054620/170314D	1
Caelo	Dexamethasone	15054629	10
Caelo	Dexamethasone	1504631	1
Caelo	Dexamethasone	17104202	1
Caelo	Dexamethasone	161001-01	1
Caelo	Dexamethasone	17104205	5
Caelo	Dexamethasone	17081716	1
Caelo	Dexamethasone	17104203	3
Caelo	Dexamethasone	17104211	20
Caelo	Dexamethasone	18121709	1
Caelo	Dexamethasone	1714203	1
Caelo	Dexamethasone	171042165511	1
Caelo	Dexamethasone	17104212	2
Caelo	Dexamethasone	111055-02	1
Caelo	Dexamethasone	11105502	1
Caelo	Dexamethasone	17332414	7
Caelo	Dexamethasone	17332415	2
Caelo	Dexamethasone	17332419	16
Caelo	Dexamethasone	13352303	1
Caelo	Dexamethasone	17332418	3
Caelo	Dexamethasone	17332417	2
Caelo	Dexamethasone	17332416	2
Caelo	Dexamethasone	19022103	3
Caelo	Dexamethasone	19022101	22
Caelo	Dexamethasone	19022107	6
Caelo	Dexamethasone	19022108	3
Caelo	Dexamethasone	19086502	10

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Supplier	Substance	Batch	Spectra
Caelo	Dexamethasone	190865001	1
Caelo	Dexamethasone	15054621	7
Caelo	Dexamethasone	12033301	3
Caelo	Dexamethasone	14196402	3
Caelo	Dexamethasone	15054610	1
Caelo	Dexamethasone	17332408	10
Caelo	Dexamethasone	17104201	1
Caelo	Dexamethasone	17104204	5
Caelo	Dexamethasone	1303007-03	1
Caelo	Dexamethasone	13084320	2
Caelo	Dexamethasone	13084304	1
Caelo	Dexamethasone	17332402	9
Caelo	Dexamethasone	17332412	7
Caelo	Dexamethasone	13084305	4
Caelo	Dexamethasone	17332415-D20180115Ma	1
Caelo	Dexamethasone	6(19086504)	1
Caelo	Dexamethasone	1504610	1
Caelo	Dexamethasone	19022112	3
Caelo	Dexamethasone	1335213	1
Caelo	Dexamethasone	17332411	1
Caelo	Dexamethasone	190022101	1
Caelo	Dexamethasone	15054606	12
Caelo	Dexamethasone	1601052-02	3
Caelo	Dexamethasone	1708004-01	8
Caelo	Dexamethasone	15054611	4
Caelo	Dexamethasone	15054603	2
Caelo	Dexamethasone	171042165585	1
Caelo	Dexamethasone	15054618	3
Caelo	Dexamethasone	13352309	1
Caelo	Dexamethasone	12033307	4
Caelo	Dexamethasone	13084310	8
Caelo	Dexamethasone	12033314	7
Caelo	Dexamethasone	13G08-N13	2
Caelo	Dexamethasone	13352311	1
Caelo	Dexamethasone	13352315	2
Caelo	Dexamethasone	15215601	1
Caelo	Dexamethasone	17104216	6
Caelo	Dexamethasone	12033318	4
Caelo	Dexamethasone	19022104	3
Caelo	Dexamethasone	10369920	8
Caelo	Dexamethasone	12033312	2
Caelo	Dexamethasone	13084306	3
Caelo	Dexamethasone	13352310	14
Caelo	Dexamethasone	1601052-01	1
Caelo	Dexamethasone	16012207	1
Caelo	Dexamethasone	19086508	1
Caelo	Dexamethasone	13084308	2
Caelo	Dexamethasone	19096503	1
Caelo	Dexamethasone	13352308	6
Caelo	Dexamethasone	17332406	5
Caelo	Dexamethasone	17332407	3
Caelo	Dexamethasone	19086501	2
Caelo	Dexamethasone	15054631	5
Caelo	Dexamethasone	13D12-N09	1
Caelo	Dexamethasone	15054622	26
Caelo	Dexamethasone	15054628	10
Caelo	Dexamethasone	1704203	1
Caelo	Dexamethasone	17104210	15
Caelo	Dexamethasone	17332403	22
Caelo	Dexamethasone	130854306	1

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Supplier	Substance	Batch	Spectra
Caelo	Dexamethasone	13352304	1
Caelo	Dexamethasone	1611001-01	3
Caelo	Dexamethasone	1704204	1
Caelo	Dexamethasone	19086504	3
Caelo	Dexamethasone	15A05-B01-304637	1
caesar	Dexamethasone	15054617	1
Caesar & Loretz GmbH	Dexamethasone	15054622	1
Caesar & Loretz GmbH	Dexamethasone	19022101	2
Caesar & Loretz GmbH	Dexamethasone	19022103	1
Caesar & Loretz GmbH	Dexamethasone	19022107	3
Caesar & Loretz GmbH	Dexamethasone	17332419	1
Caesar & Loretz GmbH	Dexamethasone	19086502	1
Caesar & Loretz GmbH / ...	Dexamethasone	17104211	2
Caesar & Loretz GmbH / ...	Dexamethasone	17332419	2
Caesar & Loretz GmbH / ...	Dexamethasone	17332416	1
Caesar & Loretz GmbH, 4...	Dexamethasone	10369922	1
Caesar & Loretz GmbH/Fi...	Dexamethasone	19086504	1
Caesar & Loretz GmbH/Ge...	Dexamethasone	19022103	1
Caesar & Loretz GmbH/Kr...	Dexamethasone	19086502	1
Caesar & Loretz/Noweda	Dexamethasone	13084319	1
caesar&lorenz GmbH,Phön...	Dexamethasone	15054622	3
Caesar&Loretz GmbH,Phön...	Dexamethasone	15054606	2
Caleo	Dexamethasone	15054602	2
calo	Dexamethasone	17332403	1
Cealo	Dexamethasone	17332404	1
Ebert-Jacobi	Dexamethasone	1611001-01	1
EuRho	Dexamethasone	1708004-01	1
EuRho / Phoenix	Dexamethasone	1303007-03	1
EuRho / Phoenix	Dexamethasone	15054631	1
EuRho Anzag	Dexamethasone	1601052-02	1
Euro OTC	Dexamethasone	1909011-01	1
Euro OTC	Dexamethasone	1111055-02	2
Euro OTC	Dexamethasone	1512211327	1
Euro OTC	Dexamethasone	DZ11005K	1
Euro OTC	Dexamethasone	1203032-01	4
Euro OTC	Dexamethasone	1203032-02	3
Euro OTC	Dexamethasone	120900802	2
Euro OTC	Dexamethasone	130300701	4
Euro OTC	Dexamethasone	130300702	2
Euro OTC	Dexamethasone	1303007-03	27
Euro OTC	Dexamethasone	1303007	1
Euro OTC	Dexamethasone	130300703	2
Euro OTC	Dexamethasone	160105202	1
Euro OTC	Dexamethasone	17104211	1
Euro OTC	Dexamethasone	17104203	1
Euro OTC	Dexamethasone	17332403	1
Euro OTC	Dexamethasone	160105201	2
Euro OTC	Dexamethasone	111105501	1
Euro OTC	Dexamethasone	180208D/1611001-01	1
Euro OTC	Dexamethasone	17080004-01	1
Euro OTC	Dexamethasone	1806023_03	1
Euro OTC	Dexamethasone	170800401	2
Euro OTC	Dexamethasone	13352309	1
Euro OTC	Dexamethasone	L53613	1
Euro OTC	Dexamethasone	1806023	1
Euro OTC	Dexamethasone	1806023-03	1
Euro OTC	Dexamethasone	1111055-01	5
Euro OTC	Dexamethasone	13030007	1
Euro OTC	Dexamethasone	1611001-01	53
Euro OTC	Dexamethasone	1303007-04	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Dexamethasone	1806023-02	9
Euro OTC	Dexamethasone	1708004-01	62
Euro OTC	Dexamethasone	1107006-01	1
Euro OTC	Dexamethasone	1806023-04	4
Euro OTC	Dexamethasone	1601052-01	24
Euro OTC	Dexamethasone	1708004-02	3
Euro OTC	Dexamethasone	13030007-01	1
Euro OTC	Dexamethasone	161100101	5
Euro OTC	Dexamethasone	T45290	2
Euro OTC	Dexamethasone	1708804-01	1
Euro OTC	Dexamethasone	700107	1
Euro OTC	Dexamethasone	5213A1327	1
Euro OTC	Dexamethasone	161101-01	1
Euro OTC	Dexamethasone	1601052-02	35
Euro OTC	Dexamethasone	1702004-01	1
Euro OTC	Dexamethasone	DB003/0213	3
Euro OTC	Dexamethasone	1209008-01	11
Euro OTC	Dexamethasone	1209008-02	26
Euro OTC	Dexamethasone	14D11-B01-294031	1
Euro OTC	Dexamethasone	17104210	1
Euro OTC	Dexamethasone	1806023-01	27
Euro OTC	Dexamethasone	180602301	2
Euro/ Sanacorp	Dexamethasone	1601052-01	2
Euro/Gehe	Dexamethasone	1708004-01	2
Euro/Gehe	Dexamethasone	1611001-01	1
Euro/Noweda	Dexamethasone	1806023-01	1
EuRoh/Fiebig	Dexamethasone	1806023-01	1
Euro OTC	Dexamethasone	15054621	1
Euro OTC	Dexamethasone	17104204	1
Euro OTC	Dexamethasone	1708004	1
Fagron	Dexamethasone	11F30-N02	1
Fagron	Dexamethasone	11L08-N01	4
Fagron	Dexamethasone	12H21-N11	2
Fagron	Dexamethasone	12B06-N12	2
Fagron	Dexamethasone	13D12-N09	3
Fagron	Dexamethasone	13D12-N19	1
Fagron	Dexamethasone	14A22-B03-290701	1
Fagron	Dexamethasone	13L30-B34-289691	2
Fagron	Dexamethasone	15a05-b01-304636	1
Fagron	Dexamethasone	1303007-03	1
Fagron	Dexamethasone	15A05-B01	1
Fagron	Dexamethasone	15054614	1
Fagron	Dexamethasone	16I06-B03-327323	3
Fagron	Dexamethasone	14A22-B03-290700	1
Fagron	Dexamethasone	16/06-B03-327323	1
Fagron	Dexamethasone	1708004-01	1
Fagron	Dexamethasone	16K24-B05-330281	1
Fagron	Dexamethasone	17E31-B01-331860	1
Fagron	Dexamethasone	17L19-B03-344100	2
Fagron	Dexamethasone	17L19-B03-344099	2
Fagron	Dexamethasone	17L19-B03	1
Fagron	Dexamethasone	18E08-B05-350243	2
Fagron	Dexamethasone	19A24-B01-359624	1
Fagron	Dexamethasone	19A24-B01	1
Fagron	Dexamethasone	15A05-B01-304636	3
Fagron	Dexamethasone	15A05-B01-304637	1
Fagron	Dexamethasone	17L19-B03-344396	1
Fagron	Dexamethasone	17104203	1
Fagron	Dexamethasone	1209008-01	1
Fagron	Dexamethasone	14D11-B01-294031	1

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Supplier	Substance	Batch	Spectra
Fagron	Dexamethasone	14A22-B03-294030	1
Fagron	Dexamethasone	15A05-B01-034636	1
Fagron	Dexamethasone	15054603	1
Fagron	Dexamethasone	16I06-B03-327488	3
Fagron	Dexamethasone	18D09-B06-348185	2
Fagron	Dexamethasone	15C16-B07	1
Fagron	Dexamethasone	NUD160702	1
Fagron	Dexamethasone	13G08-N13	3
Fagron	Dexamethasone	11D26-N10	3
Fagron	Dexamethasone	2314A-01327	1
Fagron	Dexamethasone	14D11-B01-294032	1
Fagron	Dexamethasone	19A24-B01-359625	1
Fagron	Dexamethasone	14A22-B03	2
Fagron	Dexamethasone	15C16-B07-308252	1
Fagron	Dexamethasone	15K17-B07-321457	2
Fagron	Dexamethasone	17C13-B07-332461	2
Fagron	Dexamethasone	19A24-B01-359626	1
Fagron	Dexamethasone	DZ11005K12B06-N12	1
Fagron	Dexamethasone	16K24B05330281	1
Fagron	Dexamethasone	17332414	1
Fagron	Dexamethasone	1601052-01	1
Fagron	Dexamethasone	15I04-B04-315528	1
Fagron	Dexamethasone	15/04-B04-315528	1
Fagron	Dexamethasone	17E31-B01-338016	1
Gatt-Koller	Dexamethasone	1801087	1
Gehe	Dexamethasone	1203032-02	1
Gehe	Dexamethasone	13D12-N09	2
Gehe	Dexamethasone	120900802	1
Gehe	Dexamethasone	13084317	1
Gehe	Dexamethasone	15054602	2
Gehe	Dexamethasone	15054621	1
Gehe	Dexamethasone	15054629	1
Gehe	Dexamethasone	17104212	1
Gehe	Dexamethasone	19086501	1
GEHE	Dexamethasone	17L19-B03-344099	1
GEHE	Dexamethasone	18H07-B02	1
GEHE 12.03.2014	Dexamethasone	13084306	1
Gehe 8.04.2014	Dexamethasone	13084310	2
Bombastus	Dexamethasone	1806023-01	1
Caelo	Dexamethasone	17332413	5
Caelo	Dexamethasone	19086503	16
Henry Lamotte Oils GmbH	Dexamethasone	13084304	1
Jenne	Dexamethasone	1806023-01	1
Jenne	Dexamethasone	1806023-02	1
Jenne	Dexamethasone	1909011-01	1
Kehr	Dexamethasone	17104210	1
Kehr	Dexamethasone	17104205	1
Krieger	Dexamethasone	17332406	1
L10	Dexamethasone	1708004-01	1
Noweda	Dexamethasone	12033307	2
Noweda	Dexamethasone	1303007-03	1
Noweda	Dexamethasone	17104204	1
Noweda	Dexamethasone	1708004-02	1
Noweda 02.12.2019	Dexamethasone	1806023-04	1
Caelo	Dexamethasone	15054617	11
Noweda/Apomix	Dexamethasone	1611001-01	1
Euro OTC	Dexamethasone	1303007-02	10
Fagron	Dexamethasone	700107-0002	1
PH Euro 8,0	Dexamethasone	15054610	1
Pharmacia&Upjohn Comp	Dexamethasone	1209008-02	1

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Supplier	Substance	Batch	Spectra
Pharmacia&Upjohn Compan...	Dexamethasone	1601052-02	1
Phoenix	Dexamethasone	10369928	1
Phoenix	Dexamethasone	13084313	2
Phoenix	Dexamethasone	13g08n13	1
Phoenix	Dexamethasone	15I04-B04	1
Phoenix	Dexamethasone	17332406	1
Phoenix	Dexamethasone	17332419	1
Phoenix	Dexamethasone	17332416	1
Phoenix	Dexamethasone	3405	1
Phoenix	Dexamethasone	19086503	1
Phoenix	Dexamethasone	1909011-01	1
Caelo	Dexamethasone	190901101	1
Phoenix Goettin	Dexamethasone	117113352302	1
Phönix	Dexamethasone	12033314	1
Phönix	Dexamethasone	1601052-02	3
Phönix	Dexamethasone	1708004-01	3
Phönix	Dexamethasone	1806023-01	1
PHÖNIX	Dexamethasone	15K17-B07	1
Phönix Gotha	Dexamethasone	12033315	1
Phönix Gotha	Dexamethasone	13352311	1
Caelo	Dexamethasone	16K24-B05-330281	1
Raben-Apotheke Mildenau	Dexamethasone	1303007-01	2
Sanacorp	Dexamethasone	13084308	1
Sanacorp	Dexamethasone	13352309	1
Sanacorp	Dexamethasone	1601052-01	1
Sanacorp	Dexamethasone	17332402	1
Caelo	Dexamethasone	17332404	10
Fagron	Dexamethasone	12D26-N09	2
Caelo	Dexamethasone	12033317	5
Sanofi-Chimie FR/Noweda	Dexamethasone	15054606	2
Sanofi-Chimie, FR/ Noweda	Dexamethasone	12033308	1
Symbiotica	Dexamethasone	1303007-01	1
Symbiotica	Dexamethasone	1303007-03	2
Symbiotica/Noweda	Dexamethasone	1601052-02	1
unbekannt	Dexamethasone	12D26-N09	1
Euro OTC	Dexamethasone	1303007-01	34
Caelo	Dexamethasone		3
Caelo	Dexamethasone	15054627	2
Euro OTC	Dexamethasone		2
Euro OTC	Dexamethasone	1611001	2
Fagron	Dexamethasone	19A24-B01-361445	1

- 110 090 spectra from 742 *Apo-Ident* customers from a total of 31 662 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dexamethasone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dexamethasone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	527	0	110 162
Type B	0	858	0	118 284
Type C	0	1150	7	110 090

The substance/substance group *Dexamethasone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8615 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.3007 %)
Type C	100.0000 % (> 99.8899 %)	99.3950 % (> 99.1357 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dexamethasone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Triamcinolone acetoneide	15.61	55.65
Prednisolone, micronized	19.92	58.90
Betamethasone, micronized	21.56	120.53
Prednisolon dihydrogen phosphate dinat...	26.47	—
Dexamethasone acetate	36.09	—
Fluocinolonacetoneid, micronized	41.85	—
Cyanocobalamin	43.73	—
Prednicarbate, micronized	47.41	75.17
Betamethasone valerate	49.48	95.69
Sodium edetate	52.45	—
⋮	⋮	⋮
Erythromycin	>50	68.12
Budesonide, micronized	>50	75.91
Triamcinolone, micronized	>50	84.68
Capsaicin	>50	176.13
Prednisone	>50	182.69
Heparin sodium	>50	224.14
Norethisterone acetate	>50	303.58

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dexamethasone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24504	24504	0.00	36.22
22364	22364	0.00	18.41
22914	22914	0.00	17.86
23168	21289	5.51	39.36
21850	21289	3.78	36.09
24705	24504	4.87	38.05
23169	22364	4.32	15.87
21403	21403	0.00	15.61
21289	21289	0.00	36.87

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Dexamethasone acetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20313-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dexamethasone acetate; Dexamethasoni acetat

Special notes

When selecting the *Dexamethasone acetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dexamethasone acetate	5	3	78

Second-stage model

For differentiation of the substance/substance group *Dexamethasone acetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dexamethasone acetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dexamethasone ac...	13260703	21301	40	1412430
Caelo	Dexamethasone ac...	13260706	21593	60	1502537
Caelo	Dexamethasone ac...	14200207	21815	60	20140807
Caelo	Dexamethasone ac...	14200207	21815SI	30	20140807
Euro OTC	Dexamethasone ac...	1405024-01	21614	60	20140620
Euro OTC	Dexamethasone ac...	1405024-01	21614SI	45	20140620
Euro OTC	Dexamethasone ac...	1708011	23693	40	20171002*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 335 spectra of 7 reference samples from the substance/substance group *Dexamethasone acetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 354 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 281 spectra of 8 reference samples from the substance/substance group *Dexamethasone acetate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Dexamethasone acetate	161066	22437	60
Caelo	Dexamethasone acetate	181730	24253	40
Caelo	Dexamethasone acetate	191192	24734	40
Caelo	Dexamethasone acetate	14200207	21815SI [†]	15
Caelo	Dexamethasone acetate	161066	22437SI	42
Caelo	Dexamethasone acetate	181730	24253SI	20
Caelo	Dexamethasone acetate	191192	24734SI	40
Euro OTC	Dexamethasone acetate	1708011	23693SI [†]	24

- 118861 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 231 spectra from 107 *Apo-Ident* customers from 82 batches from the substance/substance group *Dexamethasone acetate*.
- Among them are spectra of independent samples from 78 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Dexamethasone acetate	18173002	1
Caelo	Dexamethasone acetate	140502403	1
Apomix/AHD	Dexamethasone acetate	1405024-03	1
Bombastus	Dexamethasone acetate	16106616	1
Caelo	Dexamethasone acetate	11093211	1
Caelo	Dexamethasone acetate	11093215	1
Caelo	Dexamethasone acetate	12021801	2
Caelo	Dexamethasone acetate	12021814	2
Caelo	Dexamethasone acetate	13100403	5
Caelo	Dexamethasone acetate	13260705	1
Caelo	Dexamethasone acetate	14200208	1
Caelo	Dexamethasone acetate	14379607	3
Caelo	Dexamethasone acetate	14379602	2
Caelo	Dexamethasone acetate	14379611	2
Caelo	Dexamethasone acetate	14379616	5
Caelo	Dexamethasone acetate	14379615	4
Caelo	Dexamethasone acetate	16106601	1
Caelo	Dexamethasone acetate	16106608	4
Caelo	Dexamethasone acetate	16106603	5
Caelo	Dexamethasone acetate	16106607	4
Caelo	Dexamethasone acetate	16106612	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Dexamethasone acetate	16106610	1
Caelo	Dexamethasone acetate	16106611	2
Caelo	Dexamethasone acetate	16106617	4
Caelo	Dexamethasone acetate	18041813	1
Caelo	Dexamethasone acetate	1610662	1
Caelo	Dexamethasone acetate	18173002	4
Caelo	Dexamethasone acetate	18173004	2
Caelo	Dexamethasone acetate	18173001	1
Caelo	Dexamethasone acetate	18173012	5
Caelo	Dexamethasone acetate	18173007	1
Caelo	Dexamethasone acetate	191192040	1
Caelo	Dexamethasone acetate	11093210	1
Caelo	Dexamethasone acetate	14200201	3
Caelo	Dexamethasone acetate	16106616	7
Caelo	Dexamethasone acetate	16106622	2
Caelo	Dexamethasone acetate	13100407	4
Caelo	Dexamethasone acetate	13100406	1
Caelo	Dexamethasone acetate	3913Q-01326	1
Caelo	Dexamethasone acetate	50(18173001)	1
Caelo	Dexamethasone acetate	13260702	1
Caelo	Dexamethasone acetate	16106604	2
Caelo	Dexamethasone acetate	16106603/171025DM	1
Caelo	Dexamethasone acetate	14200205	3
Caelo	Dexamethasone acetate	18173011	2
Caelo	Dexamethasone acetate	161066165624	1
Caelo	Dexamethasone acetate	14379609	3
Caelo	Dexamethasone acetate	16106623	1
Caelo	Dexamethasone acetate	12021811	1
Caelo	Dexamethasone acetate	15243203	1
Caelo	Dexamethasone acetate	16106602	3
Caelo	Dexamethasone acetate	16106615	1
Caelo	Dexamethasone acetate	4113I-01326	1
Caelo	Dexamethasone acetate	13260701	4
Caelo	Dexamethasone acetate	15243201	3
Caelo	Dexamethasone acetate	14379608	1
Caelo	Dexamethasone acetate	16106613	4
Caelo	Dexamethasone acetate	19119021	1
Caelo	Dexamethasone acetate	13100404	3
Caelo	Dexamethasone acetate	13100408	2
Caelo	Dexamethasone acetate	14379601	1
Caesar & Loretz GmbH	Dexamethasone acetate	18173008	2
Caesar & Loretz GmbH	Dexamethasone acetate	18173007	2
Caesar & Loretz GmbH	Dexamethasone acetate	19119202	1
Caesar & Loretz GmbH, A...	Dexamethasone acetate	18173004	1
Caesar & Loretz GmbH, A...	Dexamethasone acetate	18173012	2
Caesar & Loretz GmbH, A...	Dexamethasone acetate	18173008	1
EuRho	Dexamethasone acetate	1110007-01	1
EuRho/Noweda	Dexamethasone acetate	1708011-01	2
Euro OTC	Dexamethasone acetate	1110007-03	1
Euro OTC	Dexamethasone acetate	1405024	1
Euro OTC	Dexamethasone acetate	140502402	1
Euro OTC	Dexamethasone acetate	1110007-01	2
Euro OTC	Dexamethasone acetate	1110007-02	5
Euro OTC	Dexamethasone acetate	1405024-02	7
Euro OTC	Dexamethasone acetate	1405024-03	16
Euro OTC	Dexamethasone acetate	1405024-04	2
Euro OTC	Dexamethasone acetate	1708011-02	2
Euro OTC	Dexamethasone acetate	1708011-01	15
europharma	Dexamethasone acetate	1110007-01	1
Fagron	Dexamethasone acetate	1110007-01	1

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Supplier	Substance	Batch	Spectra
Fagron	Dexamethasone acetate	1110007	1
Gehe	Dexamethasone acetate	16106613	1
Gehe	Dexamethasone acetate	16106619	1
Gehe	Dexamethasone acetate	18173012	1
Gehe	Dexamethasone acetate	18173007	1
Caelo	Dexamethasone acetate	16106619	3
Caelo	Dexamethasone acetate	18173008	1
Caelo	Dexamethasone acetate	15243202	4
Noweda	Dexamethasone acetate	13100406	1
Noweda	Dexamethasone acetate	1110007-02	1
Noweda	Dexamethasone acetate	1708011-02	1
Noweda	Dexamethasone acetate	18173010	1
Caelo	Dexamethasone acetate	1405024-01	1
Phönix	Dexamethasone acetate	16106603	1
Sanacorp	Dexamethasone acetate	16106613	1
Caelo	Dexamethasone acetate	12021803	3
Caelo	Dexamethasone acetate	5/AD1	1
Caelo	Dexamethasone acetate	13100401	1
Caelo	Dexamethasone acetate	22/AKD2	1
Sanofi Chimie/ Gehe	Dexamethasone acetate	18173004	1
Caelo	Dexamethasone acetate	13260703	3
Caelo	Dexamethasone acetate	14200207	1
Euro OTC	Dexamethasone acetate	1405024-01	1
Phönix	Dexamethasone acetate		1

- 111 016 spectra from 742 *Apo-Ident* customers from a total of 31 810 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dexamethasone acetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dexamethasone acetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	335	0	110 354
Type B	0	280	1	118 861
Type C	0	213	18	111 016

The substance/substance group *Dexamethasone acetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2090 %)
Type B	100.0000 % (> 99.9893 %)	99.6441 % (> 98.5765 %)
Type C	100.0000 % (> 99.8899 %)	92.2078 % (> 90.9091 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dexamethasone acetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Triamcinolone acetonide	22.72	—
Fluocinolonacetoneid, micronized	22.80	—
Dexamethasone	23.97	—
Clobetasol propionate	29.72	—
Betamethasone, micronized	36.44	—
Prednisolon dihydrogen phosphate dinat...	41.54	—
Betamethasone valerate	45.08	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dexamethasone acetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21593	21593	0.00	29.02
23693	23693	0.00	25.45
21301	21301	0.00	22.83
21614	21301	1.40	22.80
21815	21593	7.22	22.72

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Dextromethorphan hydrobromide monohydrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	22318-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dextromethorphan hydrobromide monohydrate; Dextromethorphan hydrobromidum

Special notes

When selecting the *Dextromethorphan hydrobromide monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dextromethorphan hydrobromide monohydrate	4	2	4

Second-stage model

For differentiation of the substance/substance group *Dextromethorphan hydrobromide monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dextromethorphan hydrobromide monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Dextromethorphan...	15D23-B07-308849	22318	60	AR-16-FG-008487-02
Fagron	Dextromethorphan...	15D23-B07-308849	22326	60	20150508
Fagron	Dextromethorphan...	16A22-B03-321371	23103	40	20160205
Fagron	Dextromethorphan...	17B28-B01-341594	23780	40	20170612
Fagron	Dextromethorphan...	19A08-B03-363561	24949	40	20190201

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Dextromethorphan - hydrobromide monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Dextromethorphan - hydrobromide monohydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Dextromethorphan hydrobromid...	16E23-B02-329706	23593	40
Fagron	Dextromethorphan hydrobromid...	18B09-B02-350261	24288	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 16 spectra from 6 *Apo-Ident* customers from 6 batches from the substance/substance group *Dextromethorphan hydrobromide monohydrate*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Dextromethorphan hydrobromid...	14H27-B04-299502	7
Fagron	Dextromethorphan hydrobromid...	16A22-B03-319331	1
Fagron	Dextromethorphan hydrobromid...	18B09-B02-358862	1
Phoenix	Dextromethorphan hydrobromid...	19A08-B03-363562	1
Fagron	Dextromethorphan hydrobromid...	16A22-B03-321371	5
Fagron	Dextromethorphan hydrobromid...	19A08-B03-363561	1

- 111 231 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dextromethorphan hydrobromide monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dextromethorphan hydrobromide monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	16	0	111 231

The substance/substance group *Dextromethorphan hydrobromide monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dextromethorphan hydrobromide monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	44.97	—
Estradiol hemihydrate	48.36	—
Dihydrocodeine hydrogen tartrate	53.33	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dextromethorphan hydrobromide monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22318	22318	0.00	41.99
22326	22318	1.76	41.90
23103	22318	3.04	41.10
23780	22318	5.85	41.04
24949	22318	8.76	40.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Diclofenac sodium
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20022-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Diclofenac sodium; Diclofenacum natricum

Special notes

When selecting the *Diclofenac sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Diclofenac sodium	7	3	106

Second-stage model

For differentiation of the substance/substance group *Diclofenac sodium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Diclofenac sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Diclofenac sodium	12214219	20883	20	20120815
Caelo	Diclofenac sodium	13214311	21467	60	20130826
Caelo	Diclofenac sodium	13214311	21470	60	20130826
Caelo	Diclofenac sodium	163492	23037	40	20170112*
Euro OTC	Diclofenac sodium	1403013-01	21330	40	20140401
Euro OTC	Diclofenac sodium	1607016	22694	40	20160808*
Fagron	Diclofenac sodium	13E03-N02	20886	40	20130515
Fagron	Diclofenac sodium	12L28-B05	21261	40	20130123

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 8 reference samples from the substance/substance group *Diclofenac sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 349 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Diclofenac sodium*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Diclofenac sodium	1711026	23872	40
Euro OTC	Diclofenac sodium	1904008	24618	40
Fagron	Diclofenac sodium	15D14-B04-307452	21979	60

- 119 002 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 354 spectra from 152 *Apo-Ident* customers from 112 batches from the substance/substance group *Diclofenac sodium*.
- Among them are spectra of independent samples from 105 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Diclofenac sodium	15D14B04314450	1
AHD	Diclofenac sodium	1503014-01	1
Fagron	Diclofenac sodium	18H24-B07	2
Amoli	Diclofenac sodium	1503014-01	1
Euro OTC	Diclofenac sodium	1206026	1
Bombastus	Diclofenac sodium	1711026-01	1
Caelo	Diclofenac sodium	11091201	1
Caelo	Diclofenac sodium	12214205	1
Caelo	Diclofenac sodium	12214206	1
Caelo	Diclofenac sodium	13214304	1
Caelo	Diclofenac sodium	13214303	1
Caelo	Diclofenac sodium	12214202	1
Caelo	Diclofenac sodium	140301301	1
Caelo	Diclofenac sodium	13214312	2
Caelo	Diclofenac sodium	13214316	1
Caelo	Diclofenac sodium	13214318	4
Caelo	Diclofenac sodium	5081501	1
Caelo	Diclofenac sodium	15169675	1
Caelo	Diclofenac sodium	15169617	1
Caelo	Diclofenac sodium	15K23-B03-325753	1
Caelo	Diclofenac sodium	15169613	1
Caelo	Diclofenac sodium	15278501	1
Caelo	Diclofenac sodium	16349208	1
Caelo	Diclofenac sodium	16349207	1
Caelo	Diclofenac sodium	18202602	1
Caelo	Diclofenac sodium	18202609	1
Caelo	Diclofenac sodium	17J19-B01-345397	1
Caelo	Diclofenac sodium	1711026-02	1
Caelo	Diclofenac sodium	15169604	7
Caelo	Diclofenac sodium	15K23-B03-318519	2

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Supplier	Substance	Batch	Spectra
Caelo	Diclofenac sodium	13214308	2
Caelo	Diclofenac sodium	15169609	2
Caelo	Diclofenac sodium	15169615	1
Caelo	Diclofenac sodium	15278502	2
Caelo	Diclofenac sodium	15278506	2
Caelo	Diclofenac sodium	15278507	1
Caelo	Diclofenac sodium	12L28-B05	1
Caelo	Diclofenac sodium	15K23-B03-325753	2
Caelo	Diclofenac sodium	18039202	1
Caelo	Diclofenac sodium	15278505	2
Caelo	Diclofenac sodium	13214317	5
Caelo	Diclofenac sodium	1503014-01	1
Caelo	Diclofenac sodium	13214309	3
Caelo	Diclofenac sodium	18039203	1
Caesar & Loretz GmbH	Diclofenac sodium	18202601	1
EuRho	Diclofenac sodium	1503014-01	1
Euro OTC	Diclofenac sodium	1807016-01	1
Euro OTC	Diclofenac sodium	15169606	1
EuRho/Jenne	Diclofenac sodium	1(1711026-03)	1
EuRho/Spangro	Diclofenac sodium	1711026-02	2
Euro OTC	Diclofenac sodium	13111203	1
Euro OTC	Diclofenac sodium	1206026-01	6
Euro OTC	Diclofenac sodium	25041403	1
Euro OTC	Diclofenac sodium	1403013-02	6
Euro OTC	Diclofenac sodium	11091404	1
Euro OTC	Diclofenac sodium	1403013-03	3
Euro OTC	Diclofenac sodium	12060250	1
Euro OTC	Diclofenac sodium	1607016-01	30
Euro OTC	Diclofenac sodium	15K23-B03-321673	1
Euro OTC	Diclofenac sodium	21031703	1
Euro OTC	Diclofenac sodium	1607016-02	15
Euro OTC	Diclofenac sodium	2091715	1
Euro OTC	Diclofenac sodium	23051814	1
Euro OTC	Diclofenac sodium	31101802	1
Euro OTC	Diclofenac sodium	1711026-03	19
Euro OTC	Diclofenac sodium	1711026-1	1
Euro OTC	Diclofenac sodium	17111026_01	1
Euro OTC	Diclofenac sodium	1111040-01	2
Euro OTC	Diclofenac sodium	1206026-02	3
Euro OTC	Diclofenac sodium	171102603	1
Euro OTC	Diclofenac sodium	1711026-01	13
Euro OTC	Diclofenac sodium	301180730-21	1
Euro OTC	Diclofenac sodium	140301301	1
Euro OTC	Diclofenac sodium	171102602	1
Euro OTC	Diclofenac sodium	1711026-02	9
Euro OTC	Diclofenac sodium	1711023-03	1
Euro OTC	Diclofenac sodium	12214220	1
Euro OTC	Diclofenac sodium	8051812	1
Euro OTC	Diclofenac sodium	1503014-01	12
Euro OTC	Diclofenac sodium	1607016-03	24
Euro OTC	Diclofenac sodium	17J19-B01-350960	2
Euro OTC	Diclofenac sodium	1503014-02	4
EuRoPharm/Otto	Diclofenac sodium	135796	1
EurRho/ Anzag	Diclofenac sodium	1403013-03	1
Fagron	Diclofenac sodium	14031411	1
Fagron	Diclofenac sodium	5041401	1
Fagron	Diclofenac sodium	12L28-B05-289773	2
Fagron	Diclofenac sodium	14G17-B08-297032	6
Fagron	Diclofenac sodium	10031505	1
Fagron	Diclofenac sodium	14G17B08297032	1

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Supplier	Substance	Batch	Spectra
Fagron	Diclofenac sodium	15D14-B04	1
Fagron	Diclofenac sodium	15D14-B04-314450	3
Fagron	Diclofenac sodium	15D14-B04-315835	1
Fagron	Diclofenac sodium	15K23-B03-327802	5
Fagron	Diclofenac sodium	17F02-B05-338797	6
Fagron	Diclofenac sodium	16I29	1
Fagron	Diclofenac sodium	17F02	1
Fagron	Diclofenac sodium	1607016-03	1
Fagron	Diclofenac sodium	17j19-B01-342310	1
Fagron	Diclofenac sodium	17J19-B01-350960	2
Fagron	Diclofenac sodium	17J19-B01	1
Fagron	Diclofenac sodium	17j19-b01-354796	1
Fagron	Diclofenac sodium	18H24-B07-357416	1
Fagron	Diclofenac sodium	17j19-B01-354796	1
Fagron	Diclofenac sodium	15K23-B03-324025	5
Fagron	Diclofenac sodium	17J19-B01B350960	1
Fagron	Diclofenac sodium	17J19-B01-342310	2
Fagron	Diclofenac sodium	RDS/1405/0159A	1
Fagron	Diclofenac sodium	15K23-B03-318519	2
Fagron	Diclofenac sodium	15K23-B03-321673	5
Fagron	Diclofenac sodium	15K23-B03	1
Fagron	Diclofenac sodium	16I29-B04-332372	4
Fagron	Diclofenac sodium	135796-0002	1
Fagron	Diclofenac sodium	16I29-B04	1
Fagron	Diclofenac sodium	17J19-B01-345397	1
Fagron	Diclofenac sodium	15K23-B03-325753	4
Fargon GmbH & Co.KG	Diclofenac sodium	15K23-B03-325753	1
Fargron	Diclofenac sodium	14G17-B08-297032	1
Fischar/Phönix	Diclofenac sodium	13214311	1
Gehe	Diclofenac sodium	1206026-01	1
Gehe	Diclofenac sodium	15278502	1
Gehe	Diclofenac sodium	1711026-03	1
GEHE	Diclofenac sodium	17J19-B01-342310	1
Hedinger/Phoenix	Diclofenac sodium	15278506	3
JENNE	Diclofenac sodium	17J19-B01	1
Kehr	Diclofenac sodium	1711026-03	1
L11	Diclofenac sodium	15278506	1
L12	Diclofenac sodium	18039202	1
Noweda	Diclofenac sodium	11G12-N06	1
Noweda	Diclofenac sodium	1403013-01	1
Noweda	Diclofenac sodium	15278504	1
Noweda	Diclofenac sodium	18039202	1
Phoenix	Diclofenac sodium	15K23-B03	1
Phoenix	Diclofenac sodium	1711026-02	1
Phönix	Diclofenac sodium	1403013-03	1
Phönix	Diclofenac sodium	17F02-B05-338797	1
PHÖNIX	Diclofenac sodium	17F02-B05	1
Fagron	Diclofenac sodium	17F02-B05	1
Sanacorp	Diclofenac sodium	1206026-01	1
Sanacorp	Diclofenac sodium	3616Q-02994	1
SANACORP	Diclofenac sodium	18039204	1
SANACORP	Diclofenac sodium	18202606	1
siehe Protokoll	Diclofenac sodium	15169617	1
Caelo	Diclofenac sodium	12214219	2
Caelo	Diclofenac sodium	13214311	8
Euro OTC	Diclofenac sodium	1403013-01	4
Fagron	Diclofenac sodium		1
Fagron	Diclofenac sodium	13E03-N02	1

- 110 893 spectra from 742 *Apo-Ident* customers from a total of 31 779 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Diclofenac sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Diclofenac sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	140	0	119 002
Type C	0	345	9	110 893

The substance/substance group *Diclofenac sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8899 %)	97.4576 % (> 96.6102 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Diclofenac sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fampridine	36.15	—
Phenobarbital	47.23	—
Sulfacetamide	55.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Diclofenac sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20883	23037	6.27	45.72
20886	22694	13.84	54.65
21261	22694	9.12	43.71
21330	23037	8.11	44.99
21467	23037	8.07	48.49
21470	23037	6.62	45.86
22694	22694	0.00	46.59
23037	23037	0.00	42.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Diltiazem hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20043-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Diltiazem hydrochloride; Diltiazemi hydrochloridum

Special notes

When selecting the *Diltiazem hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Diltiazem hydrochloride	4	4	343

Second-stage model

For differentiation of the substance/substance group *Diltiazem hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Diltiazem hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Diltiazem hydroc...	13346914	21300	40	20131028
Caelo	Diltiazem hydroc...	13346914	21406	60	20131028
Caelo	Diltiazem hydroc...	13346914	21407	60	20131028
Caelo	Diltiazem hydroc...	161908	22631	40	20160715*
Fagron	Diltiazem hydroc...	14C12-B04	21270	40	20140417
Fagron	Diltiazem hydroc...	16G20-B03-328133	23015	40	20160829
Fagron	Diltiazem hydroc...	16G20-B03-328133	23016	40	20160829

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Diltiazem hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 369 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Diltiazem hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Diltiazem hydrochloride	170432	23325	40
Caelo	Diltiazem hydrochloride	173370	23826	40
Caelo	Diltiazem hydrochloride	183011	24389	40
Caelo	Diltiazem hydrochloride	190841	24505	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1715 spectra from 509 *Apo-Ident* customers from 367 batches from the substance/substance group *Diltiazem hydrochloride*.
- Among them are spectra of independent samples from 344 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
11.08.14 Phoenix	Diltiazem hydrochloride	13346901	1
AHD	Diltiazem hydrochloride	14C12-B04-292757	1
AHD	Diltiazem hydrochloride	17043210	1
AHD	Diltiazem hydrochloride	17337017	2
AHD	Diltiazem hydrochloride	18301108	3
AHD	Diltiazem hydrochloride	18A29-B01-345623	2
Caelo	Diltiazem hydrochloride	17043204	9
Caelo	Diltiazem hydrochloride	19084106	7
ALH	Diltiazem hydrochloride	15414319	1
Alliance	Diltiazem hydrochloride	12133009	1
Alliance	Diltiazem hydrochloride	12133008	1
Alliance Health	Diltiazem hydrochloride	13A02-N05	1
Alliance Healthcare	Diltiazem hydrochloride	12I12-N02	1
allianz	Diltiazem hydrochloride	15230512	1
anzag	Diltiazem hydrochloride	15414319	2
Anzag	Diltiazem hydrochloride	13346915	1
Anzag	Diltiazem hydrochloride	17043203	1
Apomix/Noweda	Diltiazem hydrochloride	14C12-B04-292759	1
Bomastus / Alliance Hea...	Diltiazem hydrochloride	17043219	1
Bomastus	Diltiazem hydrochloride	16190813	1
Caelo	Diltiazem hydrochloride	14G22-B08-299781	1
Caelo	Diltiazem hydrochloride	14g22b08299781	1
Caelo	Diltiazem hydrochloride	15212802	7
Caelo	Diltiazem hydrochloride	17043230	4
Caelo	Diltiazem hydrochloride	12177101	13
Caelo	Diltiazem hydrochloride	12176801	1
Caelo	Diltiazem hydrochloride	2310213562	1
Caelo	Diltiazem hydrochloride	DIL/M-04511	1
Caelo	Diltiazem hydrochloride	12133009	7

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Supplier	Substance	Batch	Spectra
Caelo	Diltiazem hydrochloride	10212413	1
Caelo	Diltiazem hydrochloride	12176804	1
Caelo	Diltiazem hydrochloride	12/12-N02	1
Caelo	Diltiazem hydrochloride	12133011	3
Caelo	Diltiazem hydrochloride	6031302	1
Caelo	Diltiazem hydrochloride	12133014	2
Caelo	Diltiazem hydrochloride	12133022	10
Caelo	Diltiazem hydrochloride	12133028	4
Caelo	Diltiazem hydrochloride	DIL/M-19911	1
Caelo	Diltiazem hydrochloride	1319604	1
Caelo	Diltiazem hydrochloride	11091301	1
Caelo	Diltiazem hydrochloride	13196104	7
Caelo	Diltiazem hydrochloride	13196105	17
Caelo	Diltiazem hydrochloride	13196103	2
Caelo	Diltiazem hydrochloride	11134113	1
Caelo	Diltiazem hydrochloride	1334609	1
Caelo	Diltiazem hydrochloride	13A02-N05	1
Caelo	Diltiazem hydrochloride	25041401	1
Caelo	Diltiazem hydrochloride	13G16-N05	1
Caelo	Diltiazem hydrochloride	14059502	1
Caelo	Diltiazem hydrochloride	13346915	7
Caelo	Diltiazem hydrochloride	23121402	1
Caelo	Diltiazem hydrochloride	13031501	1
Caelo	Diltiazem hydrochloride	14318409	13
Caelo	Diltiazem hydrochloride	14059133	1
Caelo	Diltiazem hydrochloride	18061511	1
Caelo	Diltiazem hydrochloride	14318416	2
Caelo	Diltiazem hydrochloride	15212801	10
Caelo	Diltiazem hydrochloride	1091503	1
Caelo	Diltiazem hydrochloride	15230503	11
Caelo	Diltiazem hydrochloride	8726	1
Caelo	Diltiazem hydrochloride	15B12-B01-305399	1
Caelo	Diltiazem hydrochloride	15414302	14
Caelo	Diltiazem hydrochloride	16A18-B07-31667	1
Caelo	Diltiazem hydrochloride	140595	1
Caelo	Diltiazem hydrochloride	15230513	1
Caelo	Diltiazem hydrochloride	16A18-B07-318733	1
Caelo	Diltiazem hydrochloride	160415D	1
Caelo	Diltiazem hydrochloride	261115DHC	1
Caelo	Diltiazem hydrochloride	15414318	1
Caelo	Diltiazem hydrochloride	16190810	6
Caelo	Diltiazem hydrochloride	16190805	3
Caelo	Diltiazem hydrochloride	16G20-B03-328133	2
Caelo	Diltiazem hydrochloride	16190801	1
Caelo	Diltiazem hydrochloride	16190814	8
Caelo	Diltiazem hydrochloride	16L19-B01-330365	1
Caelo	Diltiazem hydrochloride	24061706	1
Caelo	Diltiazem hydrochloride	17043203	11
Caelo	Diltiazem hydrochloride	170432	1
Caelo	Diltiazem hydrochloride	16190818	1
Caelo	Diltiazem hydrochloride	17043216	17
Caelo	Diltiazem hydrochloride	27101706	1
Caelo	Diltiazem hydrochloride	16190815	1
Caelo	Diltiazem hydrochloride	17043217	20
Caelo	Diltiazem hydrochloride	17h25-b01340699	1
Caelo	Diltiazem hydrochloride	17043223	6
Caelo	Diltiazem hydrochloride	17043224	3
Caelo	Diltiazem hydrochloride	17H25-B01-340697	1
Caelo	Diltiazem hydrochloride	17337007	2
Caelo	Diltiazem hydrochloride	18041802	1

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Supplier	Substance	Batch	Spectra
Caelo	Diltiazem hydrochloride	12051802	1
Caelo	Diltiazem hydrochloride	23051818	1
Caelo	Diltiazem hydrochloride	17337005	20
Caelo	Diltiazem hydrochloride	17337012	17
Caelo	Diltiazem hydrochloride	17337010	5
Caelo	Diltiazem hydrochloride	1733712	1
Caelo	Diltiazem hydrochloride	17337009	27
Caelo	Diltiazem hydrochloride	27101803	1
Caelo	Diltiazem hydrochloride	17337018	16
Caelo	Diltiazem hydrochloride	17337026	14
Caelo	Diltiazem hydrochloride	17337025	16
Caelo	Diltiazem hydrochloride	17337027	11
Caelo	Diltiazem hydrochloride	18301110	9
Caelo	Diltiazem hydrochloride	19084104	6
Caelo	Diltiazem hydrochloride	19084110	3
Caelo	Diltiazem hydrochloride	1831110	1
Caelo	Diltiazem hydrochloride	13346901	8
Caelo	Diltiazem hydrochloride	15414320	1
Caelo	Diltiazem hydrochloride	1733701	1
Caelo	Diltiazem hydrochloride	19084111	2
Caelo	Diltiazem hydrochloride	15414301	18
Caelo	Diltiazem hydrochloride	15414312	1
Caelo	Diltiazem hydrochloride	170602DH/16190813	1
Caelo	Diltiazem hydrochloride	140595143	1
Caelo	Diltiazem hydrochloride	16190813	13
Caelo	Diltiazem hydrochloride	12133029	3
Caelo	Diltiazem hydrochloride	11L20-N06	1
Caelo	Diltiazem hydrochloride	16C14_B11_322642	1
Caelo	Diltiazem hydrochloride	18A29_B01_345623	1
Caelo	Diltiazem hydrochloride	19084108	5
Caelo	Diltiazem hydrochloride	15414305	4
Caelo	Diltiazem hydrochloride	15435807	1
Caelo	Diltiazem hydrochloride	14318412	18
Caelo	Diltiazem hydrochloride	17043212	1
Caelo	Diltiazem hydrochloride	17043228	5
Caelo	Diltiazem hydrochloride	17332021	1
Caelo	Diltiazem hydrochloride	18A29-B01-348861	1
Caelo	Diltiazem hydrochloride	15230000000000000000	1
Caelo	Diltiazem hydrochloride	16C14-B11-320849	1
Caelo	Diltiazem hydrochloride	16G20-B03-325903	3
Caelo	Diltiazem hydrochloride	173327027	1
Caelo	Diltiazem hydrochloride	14C12-B04-294135	1
Caelo	Diltiazem hydrochloride	19084107	4
Caelo	Diltiazem hydrochloride	19084115	2
Caelo	Diltiazem hydrochloride	1396103	1
Caelo	Diltiazem hydrochloride	18259501	1
Caelo	Diltiazem hydrochloride	13J24-B04-286569	1
Caelo	Diltiazem hydrochloride	14318403	4
Caelo	Diltiazem hydrochloride	10069509	1
Caelo	Diltiazem hydrochloride	10212404	1
Caelo	Diltiazem hydrochloride	17043202	18
Caelo	Diltiazem hydrochloride	17043218	12
Caelo	Diltiazem hydrochloride	15B12-B01-305400	1
Caelo	Diltiazem hydrochloride	13J24-B04-289432	3
Caelo	Diltiazem hydrochloride	12133008	2
Caelo	Diltiazem hydrochloride	12133023	1
Caelo	Diltiazem hydrochloride	3313U-03562	1
Caelo	Diltiazem hydrochloride	13j24-b04-286571	1
Caelo	Diltiazem hydrochloride	13346903	9
Caelo	Diltiazem hydrochloride	14059515	2

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Supplier	Substance	Batch	Spectra
Caelo	Diltiazem hydrochloride	15230501	5
Caelo	Diltiazem hydrochloride	15230515	1
Caelo	Diltiazem hydrochloride	15414310	1
Caelo	Diltiazem hydrochloride	1020617/16190813	1
Caelo	Diltiazem hydrochloride	17043207	1
Caelo	Diltiazem hydrochloride	17043210	1
Caelo	Diltiazem hydrochloride	18H09-B03-352908	1
Caelo	Diltiazem hydrochloride	17337017	1
Caelo	Diltiazem hydrochloride	19084103	1
Caelo	Diltiazem hydrochloride	15230516	1
Caelo	Diltiazem hydrochloride	16G20_B03_325903	1
Caelo	Diltiazem hydrochloride	13G16-No5	1
Caelo	Diltiazem hydrochloride	15B12-B01-305401	1
Caelo	Diltiazem hydrochloride	173337018	1
Caelo	Diltiazem hydrochloride	173337026	1
Caelo	Diltiazem hydrochloride	17043219	17
Caelo	Diltiazem hydrochloride	15230507	5
Caelo	Diltiazem hydrochloride	15230512	12
Caelo	Diltiazem hydrochloride	15414309	2
Caelo	Diltiazem hydrochloride	15414313	13
Caelo	Diltiazem hydrochloride	15414321	2
Caelo	Diltiazem hydrochloride	15414319	20
Caelo	Diltiazem hydrochloride	16A18-B07-319570	1
Caelo	Diltiazem hydrochloride	154114319	1
Caelo	Diltiazem hydrochloride	16C14-B11-322153	2
Caelo	Diltiazem hydrochloride	16190817	2
Caelo	Diltiazem hydrochloride	17043205	7
Caelo	Diltiazem hydrochloride	170729181	1
Caelo	Diltiazem hydrochloride	17053181	1
Caelo	Diltiazem hydrochloride	17043215	18
Caelo	Diltiazem hydrochloride	17D11-B11-334837	1
Caelo	Diltiazem hydrochloride	180320DHC/17043218	1
Caelo	Diltiazem hydrochloride	17337004	12
Caelo	Diltiazem hydrochloride	17337016	5
Caelo	Diltiazem hydrochloride	3442	1
Caelo	Diltiazem hydrochloride	13346902	5
Caelo	Diltiazem hydrochloride	1405904	1
Caelo	Diltiazem hydrochloride	14059503	3
Caelo	Diltiazem hydrochloride	14318410	3
Caelo	Diltiazem hydrochloride	14318413	3
Caelo	Diltiazem hydrochloride	15G20-B08-312065	2
Caelo	Diltiazem hydrochloride	16A18-B07-318732	2
Caelo	Diltiazem hydrochloride	17D11-B11-333704	1
Caelo	Diltiazem hydrochloride	17H25-B01-343273	1
Caelo	Diltiazem hydrochloride	17331012	1
Caelo	Diltiazem hydrochloride	18A29-B01-352907	1
Caelo	Diltiazem hydrochloride	18H09-B03	2
Caelo	Diltiazem hydrochloride	18H09-B03-358917	2
Caelo	Diltiazem hydrochloride	13196107	3
Caelo	Diltiazem hydrochloride	13346908	1
Caelo	Diltiazem hydrochloride	1459513	1
Caelo	Diltiazem hydrochloride	15/246/DI	1
Caelo	Diltiazem hydrochloride	14318414	3
Caelo	Diltiazem hydrochloride	1521806	1
Caelo	Diltiazem hydrochloride	15212806	2
Caelo	Diltiazem hydrochloride	15230504	3
Caelo	Diltiazem hydrochloride	15230514	2
Caelo	Diltiazem hydrochloride	16190807	3
Caelo	Diltiazem hydrochloride	17D11-B11-333705	2
Caelo	Diltiazem hydrochloride	17337011	3

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Supplier	Substance	Batch	Spectra
Caelo	Diltiazem hydrochloride	17337014	11
Caelo	Diltiazem hydrochloride	13346905	9
Caelo	Diltiazem hydrochloride	13346904	5
Caelo	Diltiazem hydrochloride	14059504	3
Caelo	Diltiazem hydrochloride	14059521	2
Caelo	Diltiazem hydrochloride	14318402	4
Caelo	Diltiazem hydrochloride	15230510	3
Caelo	Diltiazem hydrochloride	15230502	11
Caelo	Diltiazem hydrochloride	15G20-B08-314375	2
Caelo	Diltiazem hydrochloride	16190806	13
Caelo	Diltiazem hydrochloride	18301111	17
Fagron	Diltiazem hydrochloride	DIL/M-10515	2
Caecolo	Diltiazem hydrochloride	17337005	2
Caesar & Lorenz GmbH	Diltiazem hydrochloride	17043218	1
Caesar & Loretz	Diltiazem hydrochloride	16190806	1
CAESAR & LORETZ	Diltiazem hydrochloride	19084105	1
Caesar & Loretz GmbH	Diltiazem hydrochloride	12133010	1
Caesar & Loretz GmbH	Diltiazem hydrochloride	17337026	1
Caesar & Loretz GmbH	Diltiazem hydrochloride	18301111	4
Caesar & Loretz GmbH	Diltiazem hydrochloride	17337027	1
Caesar & Loretz GmbH	Diltiazem hydrochloride	17337025	4
Caesar & Loretz GmbH	Diltiazem hydrochloride	18301110	2
Caesar & Loretz GmbH	Diltiazem hydrochloride	17337018	1
Caesar & Loretz GmbH	Diltiazem hydrochloride	19084105	2
Caesar & Loretz GmbH	Diltiazem hydrochloride	19084106	3
Caesar & Loretz GmbH	Diltiazem hydrochloride	19084115	2
Caesar & Loretz GmbH / ...	Diltiazem hydrochloride	19084105	1
Caesar & Loretz GmbH / ...	Diltiazem hydrochloride	19084106	1
Caesar & Loretz GmbH/Fi...	Diltiazem hydrochloride	17337027	1
Caesar&Loretz GmbH /Anzag	Diltiazem hydrochloride	15414302	1
Caesar&Loretz GmbH/Anzag	Diltiazem hydrochloride	14318412	1
Caeser und Loretz GmbH	Diltiazem hydrochloride	19084108	1
Cealo/Sanacorp	Diltiazem hydrochloride	14059514	1
Chiesi/Phoenix	Diltiazem hydrochloride	15230502	1
Euro OTC	Diltiazem hydrochloride	17337027	1
Euro OTC	Diltiazem hydrochloride	16A18B07	1
Euro OTC	Diltiazem hydrochloride	17337005	1
Europharm / Gehe	Diltiazem hydrochloride	17H25-B01-343273	1
Fagron	Diltiazem hydrochloride	13J24-B04-286569	11
Fagron	Diltiazem hydrochloride	15B12-B01_305399	1
Fagron	Diltiazem hydrochloride	15g20-b08-314375	1
Fagron	Diltiazem hydrochloride	16A18-B07318732	1
Fagron	Diltiazem hydrochloride	11E18-N04	3
Fagron	Diltiazem hydrochloride	12D05-N070	1
Fagron	Diltiazem hydrochloride	10D28-N23	1
Fagron	Diltiazem hydrochloride	11-01-N08	1
Fagron	Diltiazem hydrochloride	612213562	1
Fagron	Diltiazem hydrochloride	12F19-N10	3
Fagron	Diltiazem hydrochloride	12I12-N02	2
Fagron	Diltiazem hydrochloride	12/12-N02	4
Fagron	Diltiazem hydrochloride	11I01-N08	1
Fagron	Diltiazem hydrochloride	12/12-N02	1
Fagron	Diltiazem hydrochloride	12K07-N02	2
Fagron	Diltiazem hydrochloride	12F19-N100102/574	1
Fagron	Diltiazem hydrochloride	13A02N05	3
Fagron	Diltiazem hydrochloride	3713M-03562	1
Fagron	Diltiazem hydrochloride	13J24-B04-286571	2
Fagron	Diltiazem hydrochloride	13J24-B04	3
Fagron	Diltiazem hydrochloride	13J24-B04-286570	1
Fagron	Diltiazem hydrochloride	14C12-B04-292757	22

continued on the next page

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Supplier	Substance	Batch	Spectra
Fagron	Diltiazem hydrochloride	13346915	1
Fagron	Diltiazem hydrochloride	22082014A	1
Fagron	Diltiazem hydrochloride	14C12B04	1
Fagron	Diltiazem hydrochloride	14C12-B04-294135	2
Fagron	Diltiazem hydrochloride	14c12-b04-292759	1
Fagron	Diltiazem hydrochloride	DIL/M-01314	1
Fagron	Diltiazem hydrochloride	14C12_B04-294133	1
Fagron	Diltiazem hydrochloride	14c12-b04-294134	1
Fagron	Diltiazem hydrochloride	14C12-B04-294134	1
Fagron	Diltiazem hydrochloride	135968-0009	2
Fagron	Diltiazem hydrochloride	14G22-B08-299781	12
Fagron	Diltiazem hydrochloride	14G22-B08299781	2
Fagron	Diltiazem hydrochloride	14G22-B08	3
Fagron	Diltiazem hydrochloride	14G22-B08-299783	1
Fagron	Diltiazem hydrochloride	14g22-b08-299781	1
Fagron	Diltiazem hydrochloride	15b12-b01-305399	2
Fagron	Diltiazem hydrochloride	15B12B01305399	2
Fagron	Diltiazem hydrochloride	14G22B08	1
Fagron	Diltiazem hydrochloride	15B12-B01-305401	3
Fagron	Diltiazem hydrochloride	15B12-B01-305299	1
Fagron	Diltiazem hydrochloride	15b12-b01-305400	2
Fagron	Diltiazem hydrochloride	15G20-B08-312065	13
Fagron	Diltiazem hydrochloride	15G20-B08	3
Fagron	Diltiazem hydrochloride	15G20-B02-310792	1
Fagron	Diltiazem hydrochloride	16A18-B07	5
Fagron	Diltiazem hydrochloride	16A18-B07-316667	11
Fagron	Diltiazem hydrochloride	2798	1
Fagron	Diltiazem hydrochloride	16A18-B07-318732	16
Fagron	Diltiazem hydrochloride	16C14-B11-320849	15
Fagron	Diltiazem hydrochloride	16C14-B11-320568	5
Fagron	Diltiazem hydrochloride	16C14B11320849	1
Fagron	Diltiazem hydrochloride	16a18-b07-318732	2
Fagron	Diltiazem hydrochloride	16C14-B11-322642	16
Fagron	Diltiazem hydrochloride	16C14B11320568	2
Fagron	Diltiazem hydrochloride	16c14-b11-211642	1
Fagron	Diltiazem hydrochloride	16A18-B07-319570	2
Fagron	Diltiazem hydrochloride	16C14-B11-322152	5
Fagron	Diltiazem hydrochloride	15414313	1
Fagron	Diltiazem hydrochloride	16A18B07316668	1
Fagron	Diltiazem hydrochloride	16C14-B11	3
Fagron	Diltiazem hydrochloride	16G20-B03	3
Fagron	Diltiazem hydrochloride	16G20-B03-325903	16
Fagron	Diltiazem hydrochloride	DIL/M-20215	1
Fagron	Diltiazem hydrochloride	17D11-B11-333704	13
Fagron	Diltiazem hydrochloride	16GH20-B03-325903	1
Fagron	Diltiazem hydrochloride	17D11-B11	5
Fagron	Diltiazem hydrochloride	17D11-B11-334837	15
Fagron	Diltiazem hydrochloride	17D11-B11-336727	5
Fagron	Diltiazem hydrochloride	16L19-B01-330395	1
Fagron	Diltiazem hydrochloride	17d11-b11-336727	1
Fagron	Diltiazem hydrochloride	17H25B01-341598	1
Fagron	Diltiazem hydrochloride	18A29-B01-345625	1
Fagron	Diltiazem hydrochloride	18a29b01345623	1
Fagron	Diltiazem hydrochloride	17H25-B01-343272	1
Fagron	Diltiazem hydrochloride	17H25-B01-341598	1
Fagron	Diltiazem hydrochloride	16G20B03-325903	1
Fagron	Diltiazem hydrochloride	16L19B01330396	1
Fagron	Diltiazem hydrochloride	18A29-B01-358861	1
Fagron	Diltiazem hydrochloride	18A29-B01-352723	2
Fagron	Diltiazem hydrochloride	18A29-B01-32907	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Diltiazem hydrochloride	18H09B03357184	1
Fagron	Diltiazem hydrochloride	18H09-B03-357184	1
Fagron	Diltiazem hydrochloride	18301110	2
Fagron	Diltiazem hydrochloride	17H25-B01-340698	2
Fagron	Diltiazem hydrochloride	18H09-B03-358917	3
Fagron	Diltiazem hydrochloride	13346902	1
Fagron	Diltiazem hydrochloride	16L19-B01	1
Fagron	Diltiazem hydrochloride	10808-N01	1
Fagron	Diltiazem hydrochloride	16L19-B01-330365	9
Fagron	Diltiazem hydrochloride	AZ-0100716	1
Fagron	Diltiazem hydrochloride	18A29-B01-352722	1
Fagron	Diltiazem hydrochloride	17H25-B01-343273	7
Fagron	Diltiazem hydrochloride	18H09-B03-358920	1
Fagron	Diltiazem hydrochloride	15B12B01305400	1
Fagron	Diltiazem hydrochloride	9J14-N17	1
Fagron	Diltiazem hydrochloride	17D11-B11-333705	3
Fagron	Diltiazem hydrochloride	18H09-B03-354798	7
Fagron	Diltiazem hydrochloride	13G16-N05	23
Fagron	Diltiazem hydrochloride	14C12-B04-292759	4
Fagron	Diltiazem hydrochloride	16g20-b03-325903	1
Fagron	Diltiazem hydrochloride	12d05-n07	1
Fagron	Diltiazem hydrochloride	17H25-B01	3
Fagron	Diltiazem hydrochloride	18H09-B03-366217	1
Fagron	Diltiazem hydrochloride	16G20-B03-328253	2
Fagron	Diltiazem hydrochloride	15G20-B08-310792	1
Fagron	Diltiazem hydrochloride	15G20-B08-314375	7
Fagron	Diltiazem hydrochloride	16L19-B01-330396	6
Fagron	Diltiazem hydrochloride	17D11-B11-334192	2
Fagron	Diltiazem hydrochloride	18A29-B01-352909	1
Fagron	Diltiazem hydrochloride	18H09-B03	6
Fagron	Diltiazem hydrochloride	AZ-0560718	3
Fagron	Diltiazem hydrochloride	13A02-N05	9
Fagron	Diltiazem hydrochloride	13F13-N05	10
Fagron	Diltiazem hydrochloride	12112-N02	1
Fagron	Diltiazem hydrochloride	DIL/M-0314	1
Fagron	Diltiazem hydrochloride	DIL/M-13114	1
Fagron	Diltiazem hydrochloride	15B12/B01305399	1
Fagron	Diltiazem hydrochloride	18A29-B01-345623	12
Fagron	Diltiazem hydrochloride	18A29-01-347886	1
Fagron	Diltiazem hydrochloride	13j24-b04-286569	1
Fagron	Diltiazem hydrochloride	14C12_B04_292757	1
Fagron	Diltiazem hydrochloride	18H09_B03_358918	1
Fagron	Diltiazem hydrochloride	18A29_B01_348861	1
Fagron	Diltiazem hydrochloride	16c14-b11-320849	1
Fagron	Diltiazem hydrochloride	17h25-b01-341596	1
Fagron	Diltiazem hydrochloride	16A14-B11-322153	1
Fagron	Diltiazem hydrochloride	17H25-B01-341596	11
Fagron	Diltiazem hydrochloride	AZ-0641216	1
Fagron	Diltiazem hydrochloride	14G22-B08-299782	6
Fagron	Diltiazem hydrochloride	15B12-B01-305399	23
Fagron	Diltiazem hydrochloride	16C14B11322152	1
Fagron	Diltiazem hydrochloride	16L19-B01_330396	1
Fagron	Diltiazem hydrochloride	17H25-B01-340699	2
Fagron	Diltiazem hydrochloride	17H25-B01-341597	2
Fagron	Diltiazem hydrochloride	18H09-B03-654798	1
Fagron	Diltiazem hydrochloride	18H-09-B03-358917	1
Fagron	Diltiazem hydrochloride	18H09_B03_354798	1
Fagron	Diltiazem hydrochloride	12D05-N07	14
Fagron	Diltiazem hydrochloride	16c14-b11-322152	1
Fagron	Diltiazem hydrochloride	18A29-B01	7

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Supplier	Substance	Batch	Spectra
Fagron	Diltiazem hydrochloride	18A29B01347886	2
Fagron	Diltiazem hydrochloride	18A29-B01-348861	16
Fagron	Diltiazem hydrochloride	18A29-B01-350964	1
Fagron	Diltiazem hydrochloride	18H09-B03-362596	1
Fagron	Diltiazem hydrochloride	18A29-B01-347886	14
Fagron	Diltiazem hydrochloride	11J28-N05	1
Fagron	Diltiazem hydrochloride	15B12-b01	1
Fagron	Diltiazem hydrochloride	15B12-B01-305400	7
Fagron	Diltiazem hydrochloride	16C14-B11-322153	6
Fagron	Diltiazem hydrochloride	16A18-B07-318733	3
Fagron	Diltiazem hydrochloride	17043203	1
Fagron	Diltiazem hydrochloride	18H09-B03-352908	1
Fagron	Diltiazem hydrochloride	18A-29-B01	1
Fagron	Diltiazem hydrochloride	DIL/M-21816	4
Fagron	Diltiazem hydrochloride	13a02-n05	1
Fagron	Diltiazem hydrochloride	13J24B04286569	3
Fagron	Diltiazem hydrochloride	14C12-B04-294133	4
Fagron	Diltiazem hydrochloride	15B12-B01	8
Fagron	Diltiazem hydrochloride	17D-11-B11-333704	1
Fagron	Diltiazem hydrochloride	17H25-B01-340697	15
Fagron	Diltiazem hydrochloride	18A29-B01-346694	6
Fagron	Diltiazem hydrochloride	18H09-B03-358918	4
Fagron	Diltiazem hydrochloride	18H09-B03-362595	1
Fargon/Kehr	Diltiazem hydrochloride	16G20-B03-328133	1
Fiebig	Diltiazem hydrochloride	15230514	5
Fiebig	Diltiazem hydrochloride	16G20-B03-328133	1
Fiebig	Diltiazem hydrochloride	17043227	1
Fiebig ek:12.27 01.08.12	Diltiazem hydrochloride	11/01-N08	1
Fragon/Noweda	Diltiazem hydrochloride	16L19-B01-330396	1
Gehe	Diltiazem hydrochloride	12133009	1
Gehe	Diltiazem hydrochloride	12133022	1
Gehe	Diltiazem hydrochloride	14C12-B04-292757	1
Gehe	Diltiazem hydrochloride	14G22-B08-299781	1
Gehe	Diltiazem hydrochloride	15414319	1
Gehe	Diltiazem hydrochloride	16190813	1
Gehe	Diltiazem hydrochloride	16190806	1
Gehe	Diltiazem hydrochloride	17043219	1
Gehe	Diltiazem hydrochloride	17337005	1
Gehe	Diltiazem hydrochloride	17043218	1
Gehe	Diltiazem hydrochloride	17337026	1
Gehe	Diltiazem hydrochloride	18301111	1
Gehe	Diltiazem hydrochloride	18H09-B03-358917	1
Gehe	Diltiazem hydrochloride	18H09-B03-358918	1
Gehe	Diltiazem hydrochloride	18H09-B03-362599	1
GEHE	Diltiazem hydrochloride	16190813	1
GEHE	Diltiazem hydrochloride	17043217	1
GEHE	Diltiazem hydrochloride	17337025	2
GEHE	Diltiazem hydrochloride	19084110	1
Caelo	Diltiazem hydrochloride	1250417	1
Caelo	Diltiazem hydrochloride	1090917/17043203	1
Fagron	Diltiazem hydrochloride	16G20B03325903	1
Fagron	Diltiazem hydrochloride	17H25-Bo1-340697	1
Fagron	Diltiazem hydrochloride	18A29-B01-346695	2
Hedinger GmbH	Diltiazem hydrochloride	16G20-B03	1
Jenne	Diltiazem hydrochloride	15414313	1
Kehr	Diltiazem hydrochloride	17043228	1
Klenk	Diltiazem hydrochloride	18A29-B01-347886	1
Klosterring	Diltiazem hydrochloride	16190806	1
Euro OTC	Diltiazem hydrochloride	17043216	1
Kuerzel	Diltiazem hydrochloride	13G16-N05	1

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Supplier	Substance	Batch	Spectra
Noweda	Diltiazem hydrochloride	12176801	1
Noweda	Diltiazem hydrochloride	12133010	1
Noweda	Diltiazem hydrochloride	12133022	1
Noweda	Diltiazem hydrochloride	12133029	1
Noweda	Diltiazem hydrochloride	13346901	1
Noweda	Diltiazem hydrochloride	14318409	1
Noweda	Diltiazem hydrochloride	15230503	1
Noweda	Diltiazem hydrochloride	15414319	1
Noweda	Diltiazem hydrochloride	16L19-B01-330365	2
Caelo	Diltiazem hydrochloride	14059513	17
Noweda 17.09.2019	Diltiazem hydrochloride	19084105	1
Fagron	Diltiazem hydrochloride	18A29-Bo1-345623	1
Caelo	Diltiazem hydrochloride	14059514	16
Caelo	Diltiazem hydrochloride	15414303	1
Caelo	Diltiazem hydrochloride	17043213	1
Fagron	Diltiazem hydrochloride	16A18B07316667	1
p&m cosmetics/gehe	Diltiazem hydrochloride	17043217	1
Caelo	Diltiazem hydrochloride	19084105	7
phoenix	Diltiazem hydrochloride	11/01-N08	1
phoenix	Diltiazem hydrochloride	14318412	1
Phoenix	Diltiazem hydrochloride	13346902	1
Phoenix	Diltiazem hydrochloride	13346914	1
Phoenix	Diltiazem hydrochloride	15230503	1
Phoenix	Diltiazem hydrochloride	17337018	1
Phoenix	Diltiazem hydrochloride	17337005	1
phönix	Diltiazem hydrochloride	14059514	1
phönix	Diltiazem hydrochloride	16G20-B03-328133	1
Phönix	Diltiazem hydrochloride	13F13-N05	1
Phönix	Diltiazem hydrochloride	13196106	1
Phönix	Diltiazem hydrochloride	15212801	1
Phönix	Diltiazem hydrochloride	15414302	1
Phönix	Diltiazem hydrochloride	17d11-b11-334837	1
Phönix	Diltiazem hydrochloride	17043219	1
Phönix	Diltiazem hydrochloride	19084106	1
PHÖNIX	Diltiazem hydrochloride	17043215	2
PHÖNIX	Diltiazem hydrochloride	17337004	2
Phönix Gotha	Diltiazem hydrochloride	15230503	1
Caelo	Diltiazem hydrochloride	12133010	12
Fagron	Diltiazem hydrochloride	18A29-B01-352907	8
Piramal Healthcare Ltd...	Diltiazem hydrochloride	12/12-N02	1
Piramal Healthcare LTD.	Diltiazem hydrochloride	12F19-N10	1
Sanacorp	Diltiazem hydrochloride	14059523	1
Caelo	Diltiazem hydrochloride	14C12-B04-294133	1
Sanacorp	Diltiazem hydrochloride	11134121	2
Sanacorp	Diltiazem hydrochloride	11134115	4
Sanacorp	Diltiazem hydrochloride	11J28-04511	1
Sanacorp	Diltiazem hydrochloride	12I12-N02	1
Sanacorp	Diltiazem hydrochloride	12133010	1
Sanacorp	Diltiazem hydrochloride	12/12-N02	2
Sanacorp	Diltiazem hydrochloride	13j24-b04-286569	1
Sanacorp	Diltiazem hydrochloride	14c12-b04-292757	1
Sanacorp	Diltiazem hydrochloride	17043217	1
Sanacorp	Diltiazem hydrochloride	17337005	1
Sanacorp WE 17.02.17 E...	Diltiazem hydrochloride	16190806	1
Sanacorp, 18.02.17, 16,...	Diltiazem hydrochloride	16190807	1
Caelo	Diltiazem hydrochloride	11134117	4
sittig	Diltiazem hydrochloride	14G22-B08-299781	1
Caelo	Diltiazem hydrochloride	12133006	1
VDL;18.02.15;15,95EUR	Diltiazem hydrochloride	14059514	1
Wepa / Wepa	Diltiazem hydrochloride	17043218	1

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Supplier	Substance	Batch	Spectra
Fagron	Diltiazem hydrochloride	16G20-B03-328133	9
Caelo	Diltiazem hydrochloride	13346914	5
Caelo	Diltiazem hydrochloride	161908	1
Fagron	Diltiazem hydrochloride	14C12-B04	7
Nachprüfung	Diltiazem hydrochloride		1
Caelo	Diltiazem hydrochloride		1

- 109 532 spectra from 742 *Apo-Ident* customers from a total of 31 526 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Diltiazem hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Diltiazem hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	160	0	118 982
Type C	0	1688	27	109 532

The substance/substance group *Diltiazem hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	98.4257 % (> 98.2507 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Diltiazem hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Benzydamine hydrochloride	34.31	—
Doxylamine hydrogen succinate	36.09	—
Cocaine hydrochloride	37.44	—
Diphenhydramine hydrochloride	46.75	—
Papaverine hydrochloride	48.11	—
Methadone hydrochloride	50.63	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Diltiazem hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23015	22631	12.20	51.75
23016	22631	14.82	49.65
21270	22631	9.84	46.26
21300	22631	5.40	45.69
21406	22631	8.13	43.67
21407	22631	5.27	45.50
22631	22631	0.00	47.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Dimethyl fumarate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21558-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dimethyl fumarate

Special notes

When selecting the *Dimethyl fumarate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dimethyl fumarate	2	1	0

Second-stage model

For differentiation of the substance/substance group *Dimethyl fumarate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dimethyl fumarate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dimethyl fumarate	13269801	21558	60	1506634
Euro OTC	Dimethyl fumarate	1410013-01	21833	60	20141125

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *Dimethyl fumarate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 569 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Dimethyl fumarate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Dimethyl fumarate	1601013-01	23907	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Dimethyl fumarate*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dimethyl fumarate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dimethyl fumarate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Dimethyl fumarate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dimethyl fumarate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Caffeine	43.32	—
Midazolam hydrochloride	66.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dimethyl fumarate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21558	21558	0.00	67.08
21833	21558	9.79	74.01

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Diphenhydramine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20186-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Diphenhydramine hydrochloride; Diphenhydramini hydrochloridum

Special notes

When selecting the *Diphenhydramine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Diphenhydramine hydrochloride	5	3	45

Second-stage model

For differentiation of the substance/substance group *Diphenhydramine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Diphenhydramine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Diphenhydramine ...	12329816	21304	40	20121119
Caelo	Diphenhydramine ...	12329816	21464	60	20121119
Caelo	Diphenhydramine ...	16004901	23235	40	20160122
Caelo	Diphenhydramine ...	180082	24755	40	20180126*
Fagron	Diphenhydramine ...	16C25-B03-331026	23262	40	AR-17-FG-015432-02
Fagron	Diphenhydramine ...	18K28-B02-358954	24702	40	20181219

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Diphenhydramine - hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Diphenhydramine - hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Diphenhydramine hydrochloride	15072617	23206	40
Caelo	Diphenhydramine hydrochloride	172276	23803	40
Caelo	Diphenhydramine hydrochloride	183010	24390	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 90 spectra from 62 *Apo-Ident* customers from 46 batches from the substance/substance group *Diphenhydramine hydrochloride*.
- Among them are spectra of independent samples from 45 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Diphenhydramine hydrochloride	12329805	1
Caelo	Diphenhydramine hydrochloride	10122030	1
Caelo	Diphenhydramine hydrochloride	5121204	1
Caelo	Diphenhydramine hydrochloride	12007702	1
Caelo	Diphenhydramine hydrochloride	25071306	1
Caelo	Diphenhydramine hydrochloride	12007713	2
Caelo	Diphenhydramine hydrochloride	2041403	1
Caelo	Diphenhydramine hydrochloride	12329815	2
Caelo	Diphenhydramine hydrochloride	31031508	1
Caelo	Diphenhydramine hydrochloride	13343104	1
Caelo	Diphenhydramine hydrochloride	13331810	2
Caelo	Diphenhydramine hydrochloride	20071502	1
Caelo	Diphenhydramine hydrochloride	13331813	1
Caelo	Diphenhydramine hydrochloride	15072603	5
Caelo	Diphenhydramine hydrochloride	15220402	1
Caelo	Diphenhydramine hydrochloride	15220405	2
Caelo	Diphenhydramine hydrochloride	15072614	9
Caelo	Diphenhydramine hydrochloride	3071715	1
Caelo	Diphenhydramine hydrochloride	16004908	2
Caelo	Diphenhydramine hydrochloride	16004910	5
Caelo	Diphenhydramine hydrochloride	18008205	1
Caelo	Diphenhydramine hydrochloride	12007715	2
Caelo	Diphenhydramine hydrochloride	1912I-01339	1
Caelo	Diphenhydramine hydrochloride	1814A-01339	1
Caelo	Diphenhydramine hydrochloride	2215I-01339	1
Caelo	Diphenhydramine hydrochloride	18008201	2
Caelo	Diphenhydramine hydrochloride	12007721	2
Caelo	Diphenhydramine hydrochloride	15072630	1
Caelo	Diphenhydramine hydrochloride	15220404	3
Caelo	Diphenhydramine hydrochloride	12007716	1

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Supplier	Substance	Batch	Spectra
Caelo	Diphenhydramine hydrochloride	13100462	1
Caelo	Diphenhydramine hydrochloride	18008208	3
Caelo	Diphenhydramine hydrochloride	15072602	3
Caelo	Diphenhydramine hydrochloride	15072609	5
Caesar & Loretz GmbH/Ph...	Diphenhydramine hydrochloride	18168407	1
Caesar/Noweda	Diphenhydramine hydrochloride	12007714	1
Fagron	Diphenhydramine hydrochloride	13A14-B40-293346	1
Fagron	Diphenhydramine hydrochloride	12J04-N02	1
Fagron	Diphenhydramine hydrochloride	12F28-N01	1
Finze	Diphenhydramine hydrochloride	9F05-N04	2
Gatt-Koller	Diphenhydramine hydrochloride	606030315	1
Caelo	Diphenhydramine hydrochloride	15072608	1
Caelo	Diphenhydramine hydrochloride	15220403	3
L30	Diphenhydramine hydrochloride	18008201	1
Noweda	Diphenhydramine hydrochloride	12007716	1
Noweda	Diphenhydramine hydrochloride	15220402	1
Caelo	Diphenhydramine hydrochloride	15072617	1
PHOENIX 29.01.2013	Diphenhydramine hydrochloride	120208	1
Phönix WE: 07.01.14 EK...	Diphenhydramine hydrochloride	12329805	1
Sanacorp	Diphenhydramine hydrochloride	12329805	1
Sanacorp	Diphenhydramine hydrochloride	15072617	1
Sanacorp	Diphenhydramine hydrochloride	16004908	1
Fagron	Diphenhydramine hydrochloride	16C25-B03-331026	1

- 111 157 spectra from 742 *Apo-Ident* customers from a total of 31 846 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Diphenhydramine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Diphenhydramine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	90	0	111 157

The substance/substance group *Diphenhydramine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 93.3333 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Diphenhydramine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cocaine hydrochloride	22.80	—
Naphazoline hydrochloride	30.43	—
Omeprazole	33.04	—
Methadone hydrochloride	42.65	—
Doxylamine hydrogen succinate	42.75	—
Benzylamine hydrochloride	47.35	—
Diltiazem hydrochloride	47.54	—
Ethyl hydrogen fumarate calcium	48.11	—
Dexamphetamine sulfate	49.72	—
Cyproterone acetate	51.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Diphenhydramine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24702	23262	5.67	25.50
21304	23262	10.99	27.00
21464	23262	8.27	24.49
23235	23262	9.06	25.84
24755	24755	0.00	31.53
23262	23262	0.00	22.80

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Dithranol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20032-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Dithranol; Dithranolum

Special notes

When selecting the *Dithranol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Dithranol	6	3	64

Second-stage model

For differentiation of the substance/substance group *Dithranol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Dithranol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Dithranol	18115302	24169	40	1811302
Caelo	Dithranol	18190604	24429	40	1904372
Caelo	Dithranol	190868	24501	40	20190426*
Caelo	Dithranol	190550	24503	40	20190426*
Euro OTC	Dithranol	1702022-01	24153	40	1809448
Fagron	Dithranol	18B23-B05-348137	24172	40	20180430

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Dithranol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 449 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Dithranol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Audor Pharma	Dithranol	APOP_DNL/11/17/001D	24173	40
Euro OTC	Dithranol	1203025-02	20873	40
Euro OTC	Dithranol	2001025	25101	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 137 spectra from 98 *Apo-Ident* customers from 70 batches from the substance/substance group *Dithranol*.
- Among them are spectra of independent samples from 63 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag	Dithranol	120302502	1
Audor Pharma	Dithranol	APDT/351/2010D	1
Audor Pharma	Dithranol	APDT3902013D	1
Audor Pharma	Dithranol	APOP-DNL11170011D	1
Audor Pharma	Dithranol	APOP-DNL/11/17/001-D	2
Audor Pharma	Dithranol	APOP-DNL/11/17/001	1
Audor Pharma	Dithranol	OP-DNL/11/17/001-1D	1
Audor Pharma	Dithranol	APOP-DNL/11/17/002D	1
Audor Pharma	Dithranol	APDT3752012D	1
Audor Pharma	Dithranol	APDT/365/2011	2
Audor Pharma	Dithranol	APDT/365/2011D	1
Audor Pharma	Dithranol	APDT/375/2012D	8
Audor Pharma	Dithranol	APOP-DNL/11/17/001-1	3
Audor Pharma	Dithranol	APOP-DNL/11/17/001D	4
Audor Pharma	Dithranol	APOP-DNL/11/17/001-1D	1
Audor Pharma	Dithranol	APD-DNL/11/17/001-1D	1
Audor Pharma	Dithranol	28 (APOP-DNL/11/17/0	1
Audor Pharma	Dithranol	DT/375/2012D	2
Audor Pharma	Dithranol	DT/351/2010D	1
Audor Pharma	Dithranol	APOP-DNL/11/17001-1	1
Audor Pharma	Dithranol	APOP-DNL/11/17/002	2
Caelo	Dithranol	1203025-02	1
Caelo	Dithranol	12014504	2
Caelo	Dithranol	27111206	1
Caelo	Dithranol	12014502	1
Caelo	Dithranol	12236809	1
Caelo	Dithranol	12375302	4
Caelo	Dithranol	12375403	1
Caelo	Dithranol	13120504	1
Caelo	Dithranol	13120702	1
Caelo	Dithranol	14101715	1
Caelo	Dithranol	18115308	1
Caelo	Dithranol	19055001	2
Caelo	Dithranol	19086804	2
Caelo	Dithranol	11064501	1

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Supplier	Substance	Batch	Spectra
Caelo	Dithranol	7/2020	1
Caelo	Dithranol	12375305	1
Caelo	Dithranol	12236811	4
Caelo	Dithranol	18115306	2
Caelo	Dithranol	192939004	1
Caelo	Dithranol	19204605	3
Caelo	Dithranol	1212I-01274	1
Caelo	Dithranol	19204604	1
Caelo	Dithranol	18B23-B05-348137	1
Caelo	Dithranol	APDT/375/2012D	3
Caelo	Dithranol	12375601	1
Caelo	Dithranol	13120502	1
Caelo	Dithranol	APOP-DNL/11/17/001-1	1
Caesar & Loretz GmbH	Dithranol	19055001	1
Caesar & Loretz GmbH	Dithranol	19086804	1
Caesar & Loretz GmbH	Dithranol	1702022-04	1
Caesar & Loretz GmbH / ...	Dithranol	192939004	1
Caesar & Loretz GmbH / ...	Dithranol	192939004	1
Caesar & Loretz GmbH / ...	Dithranol	19204605	1
EuRho	Dithranol	1203025-01	1
Euro OTC	Dithranol	1203025-01	2
Euro OTC	Dithranol	1008011-01	1
Euro OTC	Dithranol	1702021-03	1
Euro OTC	Dithranol	1311029-01	1
Euro OTC	Dithranol	1008011-02	2
Euro OTC	Dithranol	DT/370/2012	1
Euro OTC	Dithranol	2001025-01	2
Euro OTC	Dithranol	56/11072013	1
Euro OTC	Dithranol	1203025-02	14
Fagron	Dithranol	17710I-01274	1
Fagron	Dithranol	11L20-N13	1
Fagron	Dithranol	13A30-N01	4
Fagron	Dithranol	9K10-N19	1
Gehe	Dithranol	1311029-01	1
Gehe/Audar	Dithranol	APDT3752012D	1
Noweda	Dithranol	APDT/375/2012	1
Noweda	Dithranol	1203025-02	1
Noweda	Dithranol	DT/375/2012D	1
Optimus/Phönix	Dithranol	APOP-DNL11/17/002D	1
Phoenix	Dithranol	1701030-01	1
Sanacorp	Dithranol	APDT/375/2012	1
Sanacorp	Dithranol	APOP-DNL/11/17/001-D	1
Caelo	Dithranol	13120503	1
Caelo	Dithranol	APDT/3652011D	1
Audor Pharma	Dithranol		5
Caelo	Dithranol		1
Caelo	Dithranol	18115302	2
Euro OTC	Dithranol		1

- 111 110 spectra from 742 *Apo-Ident* customers from a total of 31 821 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Dithranol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dithranol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	106	14	119 022
Type C	0	103	34	111 110

The substance/substance group *Dithranol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	88.3333 % (> 85.8333 %)
Type C	100.0000 % (> 99.8899 %)	75.1825 % (> 72.9927 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dithranol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	30.23	–
Indometacin	48.53	–
L-tryptophan	50.32	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dithranol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24169	24169	0.00	67.51
24501	24501	0.00	57.60
24503	24503	0.00	68.08
24172	24503	2.59	66.50
24153	24153	0.00	57.75
24429	24429	0.00	62.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Doxycycline hyclate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20796-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Doxycycline hyclate; Doxycyclini hyclas

Special notes

When selecting the *Doxycycline hyclate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Doxycycline hyclate	4	2	19

Second-stage model

For differentiation of the substance/substance group *Doxycycline hyclate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Doxycycline hyclate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Doxycycline hycl...	12G12-N15	20796	40	1404233
Fagron	Doxycycline hycl...	12G12-N15	20821	40	20120807
Fagron	Doxycycline hycl...	14K28-B05-312218	22242	60	20150216
Fagron	Doxycycline hycl...	19A30-B01-360207	24820	40	20190412
Fagron	Doxycycline hycl...	19I12-F01-366406	24946	40	20191204

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Doxycycline hyclate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Doxycycline hyclate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Doxycycline hyclate	16I06-B02-330167	23118	40
Fagron	Doxycycline hyclate	18D18-B01-349567	24170	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 22 spectra from 15 *Apo-Ident* customers from 20 batches from the substance/substance group *Doxycycline hyclate*.
- Among them are spectra of independent samples from 19 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Doxycycline hyclate	16I06-B02-335675	1
Caelo	Doxycycline hyclate	16I06-B02-341857	1
Fagron	Doxycycline hyclate	14K28-B05-312010	1
Fagron	Doxycycline hyclate	13D24-B40-298948	1
Fagron	Doxycycline hyclate	1606B02330167	1
Fagron	Doxycycline hyclate	20101701	1
Fagron	Doxycycline hyclate	17112201	1
Fagron	Doxycycline hyclate	16/06-B02-341857	1
Fagron	Doxycycline hyclate	18D18-B01-349567	2
Fagron	Doxycycline hyclate	16E04-B07-231917	1
Fagron	Doxycycline hyclate	16106-B02-330167	1
Fagron	Doxycycline hyclate	16106-B02-330167	1
Fagron	Doxycycline hyclate	18D18_B01_349567	1
Fagron	Doxycycline hyclate	16106-Bo2	1
Fagron	Doxycycline hyclate	1603008	1
Fagron	Doxycycline hyclate	16I06-B02	1
Löwen City-Apotheke Bar...	Doxycycline hyclate	10022014	1
Löwen City-Apotheke Bar...	Doxycycline hyclate	2042015	1
Merck	Doxycycline hyclate	22022019	1
Sanacorp	Doxycycline hyclate	16I06-B02-335675	1
Fagron	Doxycycline hyclate	12G12-N15	1

- 111 225 spectra from 742 *Apo-Ident* customers from a total of 31 872 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Doxycycline hyclate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Doxycycline hyclate* and it was

evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	21	1	111 225

The substance/substance group *Doxycycline hyclate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	95.4545 % (> 81.8182 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Doxycycline hyclate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	12.32	—
Levothyroxin sodium	20.08	—
Sodium cromoglicate	38.02	—
Sodium tetraborate	48.52	—
Chloramphenicol	51.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Doxycycline hyclate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22242	20796	11.48	29.00
24820	20796	9.75	28.80
20796	20796	0.00	27.85
20821	20796	2.13	27.29
24946	20796	8.51	28.58

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Doxylamine hydrogen succinate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20315-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Doxylamine hydrogen succinate; Doxylamine succinate; Doxylamini hydrogenosuccinas

Special notes

When selecting the *Doxylamine hydrogen succinate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Doxylamine hydrogen succinate	4	2	37

Second-stage model

For differentiation of the substance/substance group *Doxylamine hydrogen succinate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Doxylamine hydrogen succinate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Doxylamine hydro...	15203906	23085	40	20151112
Caelo	Doxylamine hydro...	15203906	23086	40	20151112
Caelo	Doxylamine hydro...	183312	24535	40	20190219*
Fagron	Doxylamine hydro...	14F03-B01-293498	21542	60	1410524
Fagron	Doxylamine hydro...	15F01-B04-309189	22601	40	AR-16-FG-011361-01

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Doxylamine hydrogen succinate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Doxylamine hydrogen succinate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Doxylamine hydrogen succinate	172047	23626	40
Caelo	Doxylamine hydrogen succinate	181277	24536	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 95 spectra from 17 *Apo-Ident* customers from 38 batches from the substance/substance group *Doxylamine hydrogen succinate*.
- Among them are spectra of independent samples from 37 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Doxylamine hydrogen succinate	14k27-B07	1
Caelo	Doxylamine hydrogen succinate	15F01-B04-309189	2
Caelo	Doxylamine hydrogen succinate	15F01-B04-317385	2
Caelo	Doxylamine hydrogen succinate	15K04B01327356	1
Caesar & Loretz GmbH, 4...	Doxylamine hydrogen succinate	13A04-N02	4
Fagron	Doxylamine hydrogen succinate	11G20-N10	1
Fagron	Doxylamine hydrogen succinate	12G10-N03	6
Fagron	Doxylamine hydrogen succinate	12K21-N01	2
Fagron	Doxylamine hydrogen succinate	14F03-B01-296845	1
Fagron	Doxylamine hydrogen succinate	14K27-B07-303356	1
Fagron	Doxylamine hydrogen succinate	15F01-B04-308354	1
Fagron	Doxylamine hydrogen succinate	14F03B01293498	1
Fagron	Doxylamine hydrogen succinate	14K27-B07	1
Fagron	Doxylamine hydrogen succinate	483875887	1
Fagron	Doxylamine hydrogen succinate	18041818	1
Fagron	Doxylamine hydrogen succinate	16F06-B-02-338804	1
Fagron	Doxylamine hydrogen succinate	13E29-N03	4
Fagron	Doxylamine hydrogen succinate	12E04-N04	3
Fagron	Doxylamine hydrogen succinate	11K17-N04	3
Fagron	Doxylamine hydrogen succinate	12811328003	1
Fagron	Doxylamine hydrogen succinate	15K04-B01	1
Fagron	Doxylamine hydrogen succinate	13A04-N02	3
Fagron	Doxylamine hydrogen succinate	15K04-B01-327356	1
Fagron	Doxylamine hydrogen succinate	12811420001	1
Fagron	Doxylamine hydrogen succinate	13/26-N14	1
L10	Doxylamine hydrogen succinate	16F06B02338805	1
L10	Doxylamine hydrogen succinate	16F06-B02-341879	2
L10	Doxylamine hydrogen succinate	16F06-B02-351516	1
L12	Doxylamine hydrogen succinate	15K04-B01-327357	8
L12	Doxylamine hydrogen succinate	15K04-B01-332765	3
L12	Doxylamine hydrogen succinate	16F06-B02-338805	5
L12	Doxylamine hydrogen succinate	16F06-B02-348870	4
L12	Doxylamine hydrogen succinate	16F06-B02-353931	4
Fagron	Doxylamine hydrogen succinate	15K04-B01-318794	5
Fagron	Doxylamine hydrogen succinate	15K04-B01-317386	1
Fagron	Doxylamine hydrogen succinate	15K04-B01-322165	7

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Supplier	Substance	Batch	Spectra
Fagron	Doxylamine hydrogen succinate	16F06-B02-357986	2
L30	Doxylamine hydrogen succinate	16F06-b02-334258	1
L30	Doxylamine hydrogen succinate	16F06-B02-343936	5
Fagron	Doxylamine hydrogen succinate	15F01-B04-309189	1

- 111 152 spectra from 742 *Apo-Ident* customers from a total of 31 853 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Doxylamine hydrogen succinate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Doxylamine hydrogen succinate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	95	0	111 152

The substance/substance group *Doxylamine hydrogen succinate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 93.6842 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Doxylamine hydrogen succinate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Diltiazem hydrochloride	22.36	—
Cocaine hydrochloride	26.40	—

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Substanz	Distance in main model	Distance in second-stage model
Ethyl hydrogen fumarate calcium	38.36	—
Benzydamine hydrochloride	39.62	—
Diphenhydramine hydrochloride	40.74	—
Dexamphetamine sulfate	46.04	—
Naphazoline hydrochloride	47.65	—
Methadone hydrochloride	49.80	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Doxylamine hydrogen succinate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21542	21542	0.00	38.20
22601	22601	0.00	37.69
23085	24535	11.35	39.58
23086	24535	10.04	40.15
24535	24535	0.00	33.57

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Enalapril maleate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 10003565-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Enalapril maleate; Enalapril maleas

Special notes

When selecting the *Enalapril maleate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Enalapril maleate	2	1	0

Second-stage model

For differentiation of the substance/substance group *Enalapril maleate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Enalapril maleate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Enalapril maleate	16K14-B02-336220	23716	40	1801425
Fagron	Enalapril maleate	17J18-B03-347278	24096	40	20171208

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 80 spectra of 2 reference samples from the substance/substance group *Enalapril maleate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 609 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Enalapril maleate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Enalapril maleate	19H27-F02-364744	24945	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Enalapril maleate*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Enalapril maleate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Enalapril maleate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	110 609
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Enalapril maleate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Enalapril maleate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	82.09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Enalapril maleate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24096	23716	5.52	100.46
23716	23716	0.00	98.01

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Eosin Y**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20571-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Eosin Y; Eosinum natricum

Special notes

When selecting the *Eosin Y* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Eosin Y	4	1	27

Second-stage model

For differentiation of the substance/substance group *Eosin Y* the following second-stage model is used:

- [Submodel 8](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Eosin Y*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Eosin Y	12E25-N01	20900	60	20120607
Fagron	Eosin Y	15G01-T03-025958	22261	60	1604114
Fagron	Eosin Y	13F14-T01-017395	22534	40	1608469
Fagron	Eosin Y	13F14-T01-017395	22535	40	20141219
Fagron	Eosin Y	13F14-T01-017395	22660	40	1801115
Fagron	Eosin Y	13F14-T01-017395	22816	40	1705197
Fagron	Eosin Y	17K21-T07-042542	23975	40	1805338

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Eosin Y*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 369 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Eosin Y*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Eosin Y	13I11-N03	20932	40
Fagron	Eosin Y	13I11-N03	21208	40

- 119062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 70 spectra from 63 *Apo-Ident* customers from 32 batches from the substance/substance group *Eosin Y*.
- Among them are spectra of independent samples from 26 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Cael Sanacorp 05.02.2016	Eosin Y	13F14-T01-017395	1
Caelo	Eosin Y	12e25n01	1
Caelo	Eosin Y	15G01-T03-025958	1
Caelo	Eosin Y	13F14-T01-017395	1
Caelo	Eosin Y	14H28-M05	1
Caelo	Eosin Y	13I11-N03	1
Fagron	Eosin Y	11F21-N10	1
Fagron	Eosin Y	EYWS/16/11	2
Fagron	Eosin Y	13/11-N03	1
Fagron	Eosin Y	EYWS/15/13	1
Fagron	Eosin Y	14H28-M09	2
Fagron	Eosin Y	13fF14-T01-017395	1
Fagron	Eosin Y	17372-87-1	1
Fagron	Eosin Y	15G01-T03-027933	2
Fagron	Eosin Y	15G01-T03-034438	1
Fagron	Eosin Y	54710	1
Fagron	Eosin Y	13/11-N03	3
Fagron	Eosin Y	15G01T03025959	1
Fagron	Eosin Y	12A02-N09	2
Fagron	Eosin Y	17K21-T07-060102	4
Fagron	Eosin Y	17K21-T07_062160	1
Fagron	Eosin Y	17K21-T0-054710	1
Fagron	Eosin Y	EYWS/09/17	1
Fagron	Eosin Y	14H28-M05	4
Fagron	Eosin Y	17K21-T07-054710	5
Fagron	Eosin Y	17K21T07-054710	1
Fagron	Eosin Y	12H28-N08	3
Fargon/Sanacorp	Eosin Y	13/11-No3	1
Fiebig	Eosin Y	13F14-T01-017395	1
Gehe	Eosin Y	14H28-M05	1
L12	Eosin Y	17K21-T07-054710	1
Fagron	Eosin Y	17K21-T07-062160	1
sanacorp	Eosin Y	14H28-M05	1
Sanacorp	Eosin Y	12E25-N01	1
Fagron	Eosin Y	17K21-T07-057542	3
Fagron	Eosin Y	11E25-N01	1

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Supplier	Substance	Batch	Spectra
Caelo	Eosin Y	12e25-n01	1
Fagron	Eosin Y	12E25-N01	4
Fagron	Eosin Y	13F14-T01-017395	5
Fagron	Eosin Y	15G01-T03-025958	2
Fagron	Eosin Y	17K21-T07-042542	2

- 111 177 spectra from 742 *Apo-Ident* customers from a total of 31 859 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Eosin Y* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Eosin Y* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	80	0	119 062
Type C	0	66	4	111 177

The substance/substance group *Eosin Y* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	94.2857 % (> 90.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Eosin Y* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	27.08	—
Chlortetracycline hydrochloride	52.07	—

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Substanz	Distance in main model	Distance in second-stage model
⋮	⋮	⋮
Saccharin sodium	>50	93.84
Quinoline yellow	>50	117.98

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Eosin Y* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22261	22261	0.00	62.10
22816	22816	0.00	66.81
22534	22534	0.00	54.39
22535	22660	1.29	67.06
22660	22660	0.00	67.47
23975	23975	0.00	57.27
20900	22660	16.44	65.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ephedrine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20993-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ephedrine hydrochloride; Ephedrini hydrochloridum

Special notes

When selecting the *Ephedrine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ephedrine hydrochloride	6	1	36

Second-stage model

For differentiation of the substance/substance group *Ephedrine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ephedrine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ephedrine hydroc...	12017217	20993	40	1511635
Caelo	Ephedrine hydroc...	13323305	21322	40	20131113
Caelo	Ephedrine hydroc...	14378502	21803	60	20150106
Caelo	Ephedrine hydroc...	161197	22436	60	20160420*
Fagron	Ephedrine hydroc...	15H28-B02-316349	23073	40	20150924
Fagron	Ephedrine hydroc...	17G05-B05-337987	23927	40	20170901

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Ephedrine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Ephedrine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ephedrine hydrochloride	171736	23672	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 52 spectra from 25 *Apo-Ident* customers from 40 batches from the substance/substance group *Ephedrine hydrochloride*.
- Among them are spectra of independent samples from 36 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Ephedrine hydrochloride	10103425	1
Caelo	Ephedrine hydrochloride	11126407	1
Caelo	Ephedrine hydrochloride	12017209	2
Caelo	Ephedrine hydrochloride	12017207	1
Caelo	Ephedrine hydrochloride	12017215	1
Caelo	Ephedrine hydrochloride	12017223	1
Caelo	Ephedrine hydrochloride	13323302	1
Caelo	Ephedrine hydrochloride	14378506	2
Caelo	Ephedrine hydrochloride	14378507	1
Caelo	Ephedrine hydrochloride	16119703	1
Caelo	Ephedrine hydrochloride	16119702	1
Caelo	Ephedrine hydrochloride	1619704	1
Caelo	Ephedrine hydrochloride	10119709	1
Caelo	Ephedrine hydrochloride	16119709	1
Caelo	Ephedrine hydrochloride	16119715	3
Caelo	Ephedrine hydrochloride	18006701	2
Caelo	Ephedrine hydrochloride	18006709	1
Caelo	Ephedrine hydrochloride	18213103	1
Caelo	Ephedrine hydrochloride	13323310	1
Caelo	Ephedrine hydrochloride	151J9304	1
Caelo	Ephedrine hydrochloride	16119715200218P301	1
Caelo	Ephedrine hydrochloride	15179302	2
Caesar & Loretz GmbH	Ephedrine hydrochloride	14378503	1
Caesar & Loretz GmbH	Ephedrine hydrochloride	18213103	1
Caesar & Loretz GmbH	Ephedrine hydrochloride	18213109	1
Caesar & Loretz GmbH	Ephedrine hydrochloride	18213113	3
Caesar & Loretz GmbH, 4...	Ephedrine hydrochloride	11126411	1
Fagron	Ephedrine hydrochloride	13B19-N04	1
Fagron	Ephedrine hydrochloride	12017220	1
Fagron	Ephedrine hydrochloride	13L30-B36	1
Gatt-Koller / Phoenix	Ephedrine hydrochloride	18502141114	1
GATT-KOLLER/PHOENIX	Ephedrine hydrochloride	915/03141314	2
Gehe am 04.03.14	Ephedrine hydrochloride	13323303	1
Caelo	Ephedrine hydrochloride	13323316	1
Caelo	Ephedrine hydrochloride	14378510	1
Phoenix 04.03.14	Ephedrine hydrochloride	1332303	1
PHOENIX 10.03.2014	Ephedrine hydrochloride	13323302	1

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Supplier	Substance	Batch	Spectra
Phönix	Ephedrine hydrochloride	13323315	1
Caelo	Ephedrine hydrochloride	12017217	1
Caelo	Ephedrine hydrochloride		1
Caelo	Ephedrine hydrochloride	14378502	1
Caelo	Ephedrine hydrochloride	13323305	2

- 111 195 spectra from 742 *Apo-Ident* customers from a total of 31 852 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ephedrine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ephedrine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	40	0	119 102
Type C	0	52	0	111 195

The substance/substance group *Ephedrine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 88.4615 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ephedrine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	54.43	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ephedrine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22436	22436	0.00	56.90
23927	22436	22.25	69.13
20993	20993	0.00	56.53
21322	20993	3.01	55.25
21803	22436	2.96	55.33
23073	20993	2.96	56.72

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Epinephrine hydrogen tartrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20689-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Epinephrine hydrogen tartrate; Adrenaline hydrogen tartrate; Adrenalin tartras

Special notes

When selecting the *Epinephrine hydrogen tartrate* substance/substance group, the following information is displayed to the user:

- Advice for the identification of epinephrine bitartrate: According to the BfArM, ephedrine and its salts are considered as critical drugs in compliance to § 5 AMG. Critical drugs must not be placed on the market or be applied to humans.

Applicable documents

978-3-7692-6679-5	<i>European Pharmacopoeia 9th Edition, Basic Version 2017</i> [3]
Komm2.2.40	<i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]
AA004	<i>Erstellung und Validierung eines IdentModul-Updates</i>

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Epinephrine hydrogen tartrate	5	4	28

Second-stage model

For differentiation of the substance/substance group *Epinephrine hydrogen tartrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Epinephrine hydrogen tartrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Epinephrine hydr...	12120202	20689	40	1405614
Caelo	Epinephrine hydr...	12337804	21058	40	20121128
Caelo	Epinephrine hydr...	14007802	21489	60	1603180
Caelo	Epinephrine hydr...	14007802	21489SI	60	1603180
Caelo	Epinephrine hydr...	14007802	21490	60	20140130
Caelo	Epinephrine hydr...	14007802	21491	20	20140130
Caelo	Epinephrine hydr...	14007802	21492	20	20140130
Caelo	Epinephrine hydr...	14007802	21493	20	20140130
Caelo	Epinephrine hydr...	14007802	21494	60	20140130
Caelo	Epinephrine hydr...	14007802	21495	20	20140130
Caelo	Epinephrine hydr...	14007802	21496	20	20140130
Caelo	Epinephrine hydr...	14007802	21497	20	20140130
Caelo	Epinephrine hydr...	14007802	21498	20	20140130
Fagron	Epinephrine hydr...	12L22-N04	20749	40	20120106
Fagron	Epinephrine hydr...	18K30-B03-358514	24706	40	20190320

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 540 spectra of 15 reference samples from the substance/substance group *Epinephrine hydrogen tartrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 149 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 600 spectra of 18 reference samples from the substance/substance group *Epinephrine hydrogen tartrate*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Epinephrine hydrogen tartrate	12337805	21059	40
Caelo	Epinephrine hydrogen tartrate	162764	22777	40
Caelo	Epinephrine hydrogen tartrate	171115	23323	40
Caelo	Epinephrine hydrogen tartrate	181795	24260	40
Caelo	Epinephrine hydrogen tartrate	14007802	21490SI [†]	60
Caelo	Epinephrine hydrogen tartrate	14007802	21491SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21492SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21493SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21495SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21496SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21497SI [†]	20
Caelo	Epinephrine hydrogen tartrate	14007802	21498SI [†]	20
Caelo	Epinephrine hydrogen tartrate	162764	22777SI	40
Caelo	Epinephrine hydrogen tartrate	171115	23323SI	40
Caelo	Epinephrine hydrogen tartrate	171115	23326	40
Caelo	Epinephrine hydrogen tartrate	171115	23326SI	40
Caelo	Epinephrine hydrogen tartrate	181795	24260SI	40
Fagron	Epinephrine hydrogen tartrate	18K30-B03-358514	24706SI [†]	40

- 118 542 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 42 spectra from 25 *Apo-Ident* customers from 31 batches from the substance/substance group *Epinephrine hydrogen tartrate*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance Health 12.03.14	Epinephrine hydrogen tartrate	12337805	1
Caelo	Epinephrine hydrogen tartrate	14007808	1
Caelo	Epinephrine hydrogen tartrate	14301002	2
Caelo	Epinephrine hydrogen tartrate	15194102	1
Caelo	Epinephrine hydrogen tartrate	15239703	1
Caelo	Epinephrine hydrogen tartrate	210316-1	1
Caelo	Epinephrine hydrogen tartrate	210316-3	1
Caelo	Epinephrine hydrogen tartrate	16276402	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Epinephrine hydrogen tartrate	162746402	1
Caelo	Epinephrine hydrogen tartrate	17111503	2
Caelo	Epinephrine hydrogen tartrate	16276406	1
Caelo	Epinephrine hydrogen tartrate	123337805	1
Caelo	Epinephrine hydrogen tartrate	12337801	1
Caelo	Epinephrine hydrogen tartrate	10237109	1
Caelo	Epinephrine hydrogen tartrate	12337805	2
Caelo	Epinephrine hydrogen tartrate	15239701	2
Caelo	Epinephrine hydrogen tartrate	15194104	1
Caelo	Epinephrine hydrogen tartrate	18179504	2
Caelo	Epinephrine hydrogen tartrate	18179503	1
Fagron	Epinephrine hydrogen tartrate	12G11-N07	1
Fagron	Epinephrine hydrogen tartrate	12G11-No70076/130	1
Fagron	Epinephrine hydrogen tartrate	13I04-N03	1
Fagron	Epinephrine hydrogen tartrate	14E12-B02	1
Fagron	Epinephrine hydrogen tartrate	15A13-B02-305559	2
Fagron	Epinephrine hydrogen tartrate	16E09-B11-319882	4
Fagron	Epinephrine hydrogen tartrate	12011902	1
Fagron	Epinephrine hydrogen tartrate	13I04-N03	1
Fagron	Epinephrine hydrogen tartrate	12/02-N03	1
Fagron	Epinephrine hydrogen tartrate	16e09-b11-319882	1
GEHE	Epinephrine hydrogen tartrate	18179504	1
Phoenix 22.5.14	Epinephrine hydrogen tartrate	12337804	1
AHD 17.11.14 EK 7,60	Epinephrine hydrogen tartrate		1
Caelo	Epinephrine hydrogen tartrate	12120202	1

- 111 205 spectra from 742 *Apo-Ident* customers from a total of 31 860 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Epinephrine hydrogen tartrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Epinephrine hydrogen tartrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	540	0	110 149
Type B	0	594	6	118 542
Type C	0	42	0	111 205

The substance/substance group *Epinephrine hydrogen tartrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8889 %)
Type B	100.0000 % (> 99.9893 %)	99.0000 % (> 98.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 85.7143 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Epinephrine hydrogen tartrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	46.52	—
Neomycin sulfate	47.00	—
Levothyroxin sodium	48.83	—
Sodium cromoglicate	58.30	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Epinephrine hydrogen tartrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20689	20689	0.00	57.54
20749	21489	14.65	56.74
21058	20689	2.97	57.15
21489	21489	0.00	59.95
21490	21489	3.14	63.99
21491	21489	1.07	59.95
21492	21489	3.53	57.42
21493	21489	1.47	59.06
21494	21489	4.28	58.62
21495	21489	1.25	59.70
21496	21489	3.76	57.46
21497	20689	5.22	57.15
21498	21489	1.42	59.54
24706	20689	2.29	58.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Erythromycin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20011-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Erythromycin; Erythromycinum

Special notes

When selecting the *Erythromycin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Erythromycin	9	6	521

Second-stage model

For differentiation of the substance/substance group *Erythromycin* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Erythromycin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Erythromycin	13175601	21323	40	20130620
Caelo	Erythromycin	160792	22438	60	20160408*
Euro OTC	Erythromycin	1308016-02	21651	60	1412542
Euro OTC	Erythromycin	1508034	21890	60	20150925*
Euro OTC	Erythromycin	1607038	22832	40	20160831*
Euro OTC	Erythromycin	1705038	23438	40	20170705*
Euro OTC	Erythromycin	1811019	24420	40	20190114*
Fagron	Erythromycin	12E24-N04	21056	60	20120607
Fagron	Erythromycin	14B06-B35-290872	21669	60	20140225

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 9 reference samples from the substance/substance group *Erythromycin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 229 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 448 spectra of 9 reference samples from the substance/substance group *Erythromycin*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Erythromycin	160795	22439	60
Caelo	Erythromycin	160797	22440	60
Caelo	Erythromycin	160796	22442	60
Euro OTC	Erythromycin	1906032	24781	40
Euro OTC	Erythromycin	2002018	25121	40
Euro OTC	Erythromycin	2002038	25123	40
Caelo	Erythromycin	13175601	21323SI [†]	48
Euro OTC	Erythromycin	1508034	21890SI [†]	57
Fagron	Erythromycin	14B06-B35-290872	21669SI [†]	43

- 118694 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2762 spectra from 633 *Apo-Ident* customers from 553 batches from the substance/substance group *Erythromycin*.
- Among them are spectra of independent samples from 521 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHC 04.07.13 EK38,50	Erythromycin	12156207	1
AHD	Erythromycin	18110119-01	1
Caelo	Erythromycin	1906032-01	1
AHD 26.02.16 13,15EUR	Erythromycin	14I30-B01-308789	1
Bombastus	Erythromycin	1705038-03	1
Fagron	Erythromycin	14I30-B01-306927	3
AIH	Erythromycin	15042902	1
Alliance Health	Erythromycin	120503502	1
Alliance Healthcare	Erythromycin	12E24-N04	1
Alliance Healthcare	Erythromycin	13F12-N21	1
Alliance Healthcare	Erythromycin	1607038-02	1
Caelo	Erythromycin	18096602	3
Allianz Healthcare	Erythromycin	16079602	1
Alte Apotheke	Erythromycin	16079206	1
Fagron	Erythromycin	18F05-B01-350906	2
Anzag	Erythromycin	12152206	1
Anzag	Erythromycin	13175506	1
Anzag	Erythromycin	14044001	1
Anzag	Erythromycin	16079501	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Anzag 23.11.12 ek:26,49	Erythromycin	1205035-01	1
Apo-Ident / Phoenix	Erythromycin	EBS/1701-BM-001	1
Audor Pharma	Erythromycin	13175602	1
Audor Pharma	Erythromycin	EB022I17E	1
Audor Pharma	Erythromycin	APEB022I17E	1
Biomed	Erythromycin	1508035-01	1
Biomed/Phönix	Erythromycin	1607038-01	1
Bombastus	Erythromycin	14B06-B35-290873	1
Bombastus	Erythromycin	17088402	1
Bombastus	Erythromycin	16079606	1
Bombastus	Erythromycin	15042603	1
Bombastus	Erythromycin	14F13-B02	1
Caelo	Erythromycin	12152108	3
Caelo	Erythromycin	5042604	1
Caelo	Erythromycin	2761	1
Caelo	Erythromycin	16079702	7
Caelo	Erythromycin	27071202	1
Caelo	Erythromycin	11195407	3
Caelo	Erythromycin	1195407	1
Caelo	Erythromycin	12152105	3
Caelo	Erythromycin	11195405	1
Caelo	Erythromycin	1215219	1
Caelo	Erythromycin	20270912-3	1
Caelo	Erythromycin	12152202	3
Caelo	Erythromycin	12152205	10
Caelo	Erythromycin	3110195	1
Caelo	Erythromycin	12E24-N04	1
Caelo	Erythromycin	12152101	3
Caelo	Erythromycin	12152206	8
Caelo	Erythromycin	13A02-N06	1
Caelo	Erythromycin	22041302	1
Caelo	Erythromycin	12152201	7
Caelo	Erythromycin	12152208	4
Caelo	Erythromycin	13D30-N01	3
Caelo	Erythromycin	19071306	1
Caelo	Erythromycin	12156206	2
Caelo	Erythromycin	1008018-02	1
Caelo	Erythromycin	13175501	6
Caelo	Erythromycin	13189007	1
Caelo	Erythromycin	13189006	3
Caelo	Erythromycin	13175506	4
Caelo	Erythromycin	12152107	1
Caelo	Erythromycin	13175503	8
Caelo	Erythromycin	24101312	1
Caelo	Erythromycin	13175604	7
Caelo	Erythromycin	511111	1
Caelo	Erythromycin	20122013D	1
Caelo	Erythromycin	26011402	1
Caelo	Erythromycin	13175607	8
Caelo	Erythromycin	13175612	2
Caelo	Erythromycin	13175804	2
Caelo	Erythromycin	13178756tzgklhj	1
Caelo	Erythromycin	13175811	8
Caelo	Erythromycin	1114Q-01362	1
Caelo	Erythromycin	14044001	10
Caelo	Erythromycin	24071402	1
Caelo	Erythromycin	13175611	5
Caelo	Erythromycin	14044004	11
Caelo	Erythromycin	3092014B	1
Caelo	Erythromycin	14044009	2

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Supplier	Substance	Batch	Spectra
Caelo	Erythromycin	14b06-b35-293508	1
Caelo	Erythromycin	14044002	10
Caelo	Erythromycin	28101405	1
Caelo	Erythromycin	14044010	4
Caelo	Erythromycin	14044105	4
Caelo	Erythromycin	14044107	3
Caelo	Erythromycin	30011505	1
Caelo	Erythromycin	14044006	6
Caelo	Erythromycin	14044101	7
Caelo	Erythromycin	14044115	6
Caelo	Erythromycin	140440006	1
Caelo	Erythromycin	14044109	5
Caelo	Erythromycin	28041505	1
Caelo	Erythromycin	5052015D	1
Caelo	Erythromycin	1430b01300059	1
Caelo	Erythromycin	140044203	1
Caelo	Erythromycin	14044206	2
Caelo	Erythromycin	1409019-01	2
Caelo	Erythromycin	14044014	3
Caelo	Erythromycin	14044207	2
Caelo	Erythromycin	1404418	1
Caelo	Erythromycin	15042602	6
Caelo	Erythromycin	15042605	6
Caelo	Erythromycin	10091502	1
Caelo	Erythromycin	14/30-B01-308189	2
Caelo	Erythromycin	15042604	3
Caelo	Erythromycin	15042701	11
Caelo	Erythromycin	15042703	9
Caelo	Erythromycin	15042613	4
Caelo	Erythromycin	1404414	1
Caelo	Erythromycin	15042707	1
Caelo	Erythromycin	15042606	1
Caelo	Erythromycin	140901902	2
Caelo	Erythromycin	1524002	1
Caelo	Erythromycin	15042711	13
Caelo	Erythromycin	15245003	8
Caelo	Erythromycin	15042803	13
Caelo	Erythromycin	15042802	3
Caelo	Erythromycin	3081601	1
Caelo	Erythromycin	15042808	1
Caelo	Erythromycin	15245008	3
Caelo	Erythromycin	15042608	3
Caelo	Erythromycin	15042809	3
Caelo	Erythromycin	15042811	3
Caelo	Erythromycin	15042804	1
Caelo	Erythromycin	150428	1
Caelo	Erythromycin	16G06-B03-324464	2
Caelo	Erythromycin	16079202	7
Caelo	Erythromycin	140930E	1
Caelo	Erythromycin	15042902	2
Caelo	Erythromycin	1504812	1
Caelo	Erythromycin	16G06-B03-324465	1
Caelo	Erythromycin	1607038-01	3
Caelo	Erythromycin	1504813	1
Caelo	Erythromycin	15042901	9
Caelo	Erythromycin	16079208	6
Caelo	Erythromycin	15042816	6
Caelo	Erythromycin	16079204	13
Caelo	Erythromycin	15042812	1
Caelo	Erythromycin	4316E-01362	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Erythromycin	16079210	8
Caelo	Erythromycin	23021710	1
Caelo	Erythromycin	16079501	15
Caelo	Erythromycin	16079205	4
Caelo	Erythromycin	1607038-02	7
Caelo	Erythromycin	16079216	8
Caelo	Erythromycin	16079511	8
Caelo	Erythromycin	150242813	1
Caelo	Erythromycin	16079502	12
Caelo	Erythromycin	16079507	1
Caelo	Erythromycin	16079510	6
Caelo	Erythromycin	16079515	1
Caelo	Erythromycin	16079503	5
Caelo	Erythromycin	160796	1
Caelo	Erythromycin	16079604	5
Caelo	Erythromycin	16079612	13
Caelo	Erythromycin	16091712	1
Caelo	Erythromycin	16079509	10
Caelo	Erythromycin	16079607	1
Caelo	Erythromycin	16079609	7
Caelo	Erythromycin	16079704	2
Caelo	Erythromycin	1708808	1
Caelo	Erythromycin	17088007	8
Caelo	Erythromycin	16079610	1
Caelo	Erythromycin	17088004	11
Caelo	Erythromycin	16G06-B03-324466	1
Caelo	Erythromycin	17088010	13
Caelo	Erythromycin	13011810	1
Caelo	Erythromycin	17219705	1
Caelo	Erythromycin	17088013	20
Caelo	Erythromycin	17088405	10
Caelo	Erythromycin	17088011	1
Caelo	Erythromycin	12051801	1
Caelo	Erythromycin	17088203	11
Caelo	Erythromycin	178824	1
Caelo	Erythromycin	170718A	1
Caelo	Erythromycin	170880103	1
Caelo	Erythromycin	1709038-01	1
Caelo	Erythromycin	1091801	1
Caelo	Erythromycin	16J24-B-341876	1
Caelo	Erythromycin	1780210	1
Caelo	Erythromycin	17088208	2
Caelo	Erythromycin	17088210	17
Caelo	Erythromycin	17088207	6
Caelo	Erythromycin	17088308	6
Caelo	Erythromycin	17088304	1
Caelo	Erythromycin	19011908	1
Caelo	Erythromycin	170503802	1
Caelo	Erythromycin	17068309	1
Caelo	Erythromycin	180962011905013-04	1
Caelo	Erythromycin	18096208	8
Caelo	Erythromycin	18096209	10
Caelo	Erythromycin	13175502	4
Caelo	Erythromycin	14I30-B01	1
Caelo	Erythromycin	17088003	9
Caelo	Erythromycin	11195306	1
Caelo	Erythromycin	14044202	3
Caelo	Erythromycin	1308016-01	2
Caelo	Erythromycin	14044012	2
Caelo	Erythromycin	17088008-20180206Ma2	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Erythromycin	16J24-B10-341876	1
Caelo	Erythromycin	16J24-B10-341875	1
Caelo	Erythromycin	17088406	6
Caelo	Erythromycin	16079214-20171127Ma6	1
Caelo	Erythromycin	17088008-E20180112Ma	1
Caelo	Erythromycin	17088010-20180404Ma2	1
Caelo	Erythromycin	180096302	1
Caelo	Erythromycin	12152109	10
Caelo	Erythromycin	132152108	1
Caelo	Erythromycin	13H22-N07	1
Caelo	Erythromycin	15042610	10
Caelo	Erythromycin	15042815	3
Caelo	Erythromycin	16979201	1
Caelo	Erythromycin	1205036-01	2
Caelo	Erythromycin	12156203	2
Caelo	Erythromycin	140440044	1
Caelo	Erythromycin	12152203	1
Caelo	Erythromycin	16079605	2
Caelo	Erythromycin	17088302	2
Caelo	Erythromycin	18096202	8
Caelo	Erythromycin	1414M-01362	1
Caelo	Erythromycin	18095303	1
Caelo	Erythromycin	150427704	1
Caelo	Erythromycin	16079603	8
Caelo	Erythromycin	11195402	3
Caelo	Erythromycin	1705038_02	1
Caelo	Erythromycin	13175803	7
Caelo	Erythromycin	15245002	17
Caelo	Erythromycin	1308016-02	1
Caelo	Erythromycin	13189002	7
Caelo	Erythromycin	14044205	4
Caelo	Erythromycin	15042611-20160504Ma1	1
Caelo	Erythromycin	17088210-E20181115Ma	1
Caelo	Erythromycin	17088403-E2081115Ma1	1
Caelo	Erythromycin	16079214-20170704Ma1	1
Caelo	Erythromycin	17088204	30
Caelo	Erythromycin	13175808	2
Caelo	Erythromycin	14044011	2
Caelo	Erythromycin	17088212	1
Caelo	Erythromycin	18096201	9
Caelo	Erythromycin	15042806	11
Caelo	Erythromycin	15042814	10
Caelo	Erythromycin	15245007	2
Caelo	Erythromycin	1524004	1
Caelo	Erythromycin	1708807	1
Caelo	Erythromycin	17088403	17
Caelo	Erythromycin	18096303	6
Caelo	Erythromycin	18096403	1
Caelo	Erythromycin	16079213	11
Caelo	Erythromycin	16079514	1
Caelo	Erythromycin	3317	1
Caelo	Erythromycin	18096404	2
Caelo	Erythromycin	15042603	5
Caelo	Erythromycin	15042704	9
Caelo	Erythromycin	17088301	41
Caelo	Erythromycin	1705038-02	1
Caelo	Erythromycin	12156204	4
Caelo	Erythromycin	16079513	9
Caelo	Erythromycin	17088306	20
Caelo	Erythromycin	18096211	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Erythromycin	15042702	4
Caelo	Erythromycin	150803401	1
Caelo	Erythromycin	1708/8308	1
Caelo	Erythromycin	16079203	18
Caelo	Erythromycin	14044114	5
Caelo	Erythromycin	14044118	3
Caelo	Erythromycin	12156208	6
Caelo	Erythromycin	13189001	7
Caelo	Erythromycin	14/30-B01-300059	1
Caelo	Erythromycin	14044201	5
Caelo	Erythromycin	14F13-B02-300061	1
Caelo	Erythromycin	1811019-02	1
Caelo	Erythromycin	13175603	11
Caelo	Erythromycin	13175801	10
Caelo	Erythromycin	14B06-B35-290873	1
Caelo	Erythromycin	13175810	3
Caelo	Erythromycin	15042601	2
Caelo	Erythromycin	1508034-02	3
Caelo	Erythromycin	1705038-01	3
Caelo	Erythromycin	17088005	4
Caelo	Erythromycin	18096203	1
Caelo	Erythromycin	16073038-02	1
Caelo	Erythromycin	17088403-20180619Ma1	1
Caelo	Erythromycin	13175504	6
Caelo	Erythromycin	16079701	1
Caelo	Erythromycin	131756017	1
Caelo	Erythromycin	17088002	15
Caelo	Erythromycin	12156207	3
Caelo	Erythromycin	13145504	1
Caelo	Erythromycin	13175608	5
Caelo	Erythromycin	13175809	5
Caelo	Erythromycin	14044007	7
Caelo	Erythromycin	14F13-B02-296464	2
Caelo	Erythromycin	EB06/14	1
Caelo	Erythromycin	1409019-02	4
Caelo	Erythromycin	15245101	10
Caelo	Erythromycin	16079201	7
Caelo	Erythromycin	16079602	4
Caelo	Erythromycin	16079506	4
Caelo	Erythromycin	16079608	16
Fagron	Erythromycin	17088211	1
Caelo	Erythromycin	12156201	3
Caelo	Erythromycin	1404409	1
Caelo	Erythromycin	14044110	1
Caelo	Erythromycin	15042612	6
Caelo	Erythromycin	15042609	8
Caelo	Erythromycin	15245004	11
Caelo	Erythromycin	15245005	1
Caelo	Erythromycin	16079505	3
Caelo	Erythromycin	16079214	9
Caelo	Erythromycin	16079512	4
Caelo	Erythromycin	16079606	6
Caelo	Erythromycin	16079614	5
Caelo	Erythromycin	17088009	7
Caelo	Erythromycin	17088401	1
Caelo	Erythromycin	17088305	13
Caelo	Erythromycin	18096302	4
Caelo	Erythromycin	18096406	7
Caelo	Erythromycin	1315501	1
Caelo	Erythromycin	13175802	8

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Erythromycin	14044106	1
Caelo	Erythromycin	154042602	1
Caelo	Erythromycin	15042706	9
Caelo	Erythromycin	15042611	5
Caelo	Erythromycin	15042813	11
Caelo	Erythromycin	10079203	1
Caelo	Erythromycin	16079207	5
Caelo	Erythromycin	1705038	2
Caelo	Erythromycin	17088001	3
Caelo	Erythromycin	1705037-01	1
Caelo	Erythromycin	16i24-B10	1
Caelo	Erythromycin	17088309	7
Caelo	Erythromycin	18096210	1
Caelo	Erythromycin	15042810	4
Caelo	Erythromycin	13175504-3413310132	1
Caelo	Erythromycin	13175505	3
Caelo	Erythromycin	13175506-3559412014	1
Caelo	Erythromycin	14044005	8
Caelo	Erythromycin	1508034-01	1
Caelo	Erythromycin	16G06-803	1
Caelo	Erythromycin	16G06B03329150	1
Caelo	Erythromycin	17088402	6
Caelo	Erythromycin	1788402	1
Caelo	Erythromycin	18096401	6
Caeolo/Krieger	Erythromycin	17088004	1
Caeolo/Noweda	Erythromycin	13189007	1
Caesar & Loretz GmbH	Erythromycin	15042814	1
Caesar & Loretz GmbH	Erythromycin	17088308	1
Caesar & Loretz GmbH	Erythromycin	17088306	3
Caesar & Loretz GmbH	Erythromycin	18096204	1
Caesar & Loretz GmbH	Erythromycin	17088309	1
Caesar & Loretz GmbH	Erythromycin	17088404	2
Caesar & Loretz GmbH	Erythromycin	18096205	3
Caesar & Loretz GmbH	Erythromycin	18096201	1
Caesar & Loretz GmbH	Erythromycin	18096208	1
Caesar & Loretz GmbH	Erythromycin	18096203	1
Caesar & Loretz GmbH	Erythromycin	18096209	1
Caesar & Loretz GmbH	Erythromycin	18096210	3
Caesar & Loretz GmbH	Erythromycin	18096211	1
Caesar & Loretz GmbH	Erythromycin	18096401	2
Caesar & Loretz GmbH	Erythromycin	18096406	1
Caesar & Loretz GmbH	Erythromycin	18096305	1
Caesar & Loretz GmbH / ...	Erythromycin	17088404	1
Caesar & Loretz GmbH / ...	Erythromycin	18096201	1
Caesar & Loretz GmbH / ...	Erythromycin	18096208	1
Caesar & Loretz GmbH / ...	Erythromycin	18096406	1
Caesar & Loretz GmbH / ...	Erythromycin	18096406	1
Caesar & Loretz GmbH, 4...	Erythromycin	10217208	1
Caesar & Loretz GmbH, 4...	Erythromycin	13189002	1
Caesar & Loretz GmbH, P...	Erythromycin	17088003	1
Caesar & Loretz GmbH, P...	Erythromycin	16079207	1
Caesar & Loretz GmbH/ G	Erythromycin	18096201	1
Caesar & Loretz GmbH/ GTH	Erythromycin	18096209	1
Caesar & Loretz GmbH/Al...	Erythromycin	17088303	1
Caesar & Loretz/AHC	Erythromycin	15042813	1
Caesar & Loretz/Sanacorp	Erythromycin	18096201	2
Caesar u. Loretz/Noweda	Erythromycin	16079209	1
Caesar&Loretz GmbH	Erythromycin	15042807	1
Caesar&Loretz GmbH /Anzag	Erythromycin	15042610	1
Caesar&loretz,Phoenix	Erythromycin	13175602	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar&loretz,Phoenix	Erythromycin	14044004	1
caesar&loretz,phönix	Erythromycin	15042603	1
Caesar/Loretz/Noweda	Erythromycin	15042610	1
Calo/AHD	Erythromycin	15042605	1
Cealo / Noweda	Erythromycin	1205036-02	1
Cealo/Alliance Healthcare	Erythromycin	17088309	1
Celo/Kehr	Erythromycin	16079608	1
Eigenherstellung	Erythromycin	14044006	1
EuRho	Erythromycin	1205035-01	1
EuRho	Erythromycin	1205035-02	1
EuRho	Erythromycin	1205036-01	1
EuRho	Erythromycin	1308016-02	2
EuRho	Erythromycin	1705038-03	1
EuRho	Erythromycin	1705038-01	1
EuRho 08.08.2013Allianc...	Erythromycin	1205036-01	1
EuRho/Noweda	Erythromycin	1508034-02	1
EuRho/Noweda	Erythromycin	1705038-01	1
EuRho/Phönix	Erythromycin	1106036-05	1
EuRho/Phönix	Erythromycin	1205035	1
EuRho/Phönix	Erythromycin	1308016-02	1
EuRho/Phönix	Erythromycin	1811019-01	1
Euro	Erythromycin	1308016-02	1
Euro CT Phönix	Erythromycin	13175604	1
Euro Oct/Phoenix	Erythromycin	1705038-03	1
EURO OGT / Anzag	Erythromycin	1409019-01	1
Euro OT	Erythromycin	1409019-02	1
Euro OTC	Erythromycin	1409019-01	27
Euro OTC	Erythromycin	1705038-02	16
Euro OTC	Erythromycin	1106036-05	6
Euro OTC	Erythromycin	1205035-02	17
Euro OTC	Erythromycin	4112Q-01362	1
Euro OTC	Erythromycin	1013u-01362	1
Euro OTC	Erythromycin	120503602	2
Euro OTC	Erythromycin	1308016-01	28
Euro OTC	Erythromycin	120503502	1
Euro OTC	Erythromycin	1409019-01Mg100g	1
Euro OTC	Erythromycin	1409019-02	45
Euro OTC	Erythromycin	1508034-02	14
Euro OTC	Erythromycin	15042810	1
Euro OTC	Erythromycin	15245008	1
Euro OTC	Erythromycin	1607038-01	69
Euro OTC	Erythromycin	167038-01	1
Euro OTC	Erythromycin	1906032-01	5
Euro OTC	Erythromycin	1811019_02	1
Euro OTC	Erythromycin	170538-03	1
Euro OTC	Erythromycin	17088203	2
Euro OTC	Erythromycin	160703802	2
Euro OTC	Erythromycin	17088210	4
Euro OTC	Erythromycin	1811019-02	3
Euro OTC	Erythromycin	1607038/01	1
Euro OTC	Erythromycin	700770	1
Euro OTC	Erythromycin	1409019-02Gehe	1
Euro OTC	Erythromycin	150834-01	1
Euro OTC	Erythromycin	15080-01	1
Euro OTC	Erythromycin	80616-4	1
Euro OTC	Erythromycin	1607038-02	62
Euro OTC	Erythromycin	1705038-01	98
Euro OTC	Erythromycin	EBS/1701-BM-001	3
Euro OTC	Erythromycin	170503801	1
Euro OTC	Erythromycin	1106036-04	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Erythromycin	1205035-01	13
Euro OTC	Erythromycin	120503601	1
Euro OTC	Erythromycin	1205036/02	1
Euro OTC	Erythromycin	EBS/1205-M-040	1
Euro OTC	Erythromycin	14044205	1
Euro OTC	Erythromycin	95(1705038-02	1
Euro OTC	Erythromycin	97(1811019-02)	1
Euro OTC	Erythromycin	1508034-02Mg100g	1
Euro OTC	Erythromycin	1811019-01	42
Euro OTC	Erythromycin	96(1811019-01)	1
Euro OTC	Erythromycin	180201E/1705038-01	1
Euro OTC	Erythromycin	3613A1362	1
Euro OTC	Erythromycin	1508034-01	35
Euro OTC	Erythromycin	181119-01	1
Euro OTC	Erythromycin	150803401	1
Euro OTC	Erythromycin	16079206	1
Euro OTC	Erythromycin	1705038_01	1
Euro OTC	Erythromycin	140901902	1
Euro OTC	Erythromycin	EBS/1307-BM-001	1
Euro OTC	Erythromycin	18111019	1
Euro OTC	Erythromycin	1705038-03	20
Euro OTC	Erythromycin	14090-9-01	1
Euro/ANZAG	Erythromycin	1705038-03	1
Euro/Gehe	Erythromycin	1508034-01	1
euroct/gehe	Erythromycin	1308016-02	2
euroct/gehe	Erythromycin	1308016-01	1
Euroct/Gehe	Erythromycin	1409019-01	2
Euro OTC	Erythromycin	12A02-N06	1
Euro OTC	Erythromycin	1607038-2	1
Euro OTC	Erythromycin	130801602	2
Euro OTC	Erythromycin	130801601	6
Euro OTC	Erythromycin	1205036-02	9
Europharm/Otto	Erythromycin	1106036-05	2
EuroTOC / Noweda	Erythromycin	1409019-02	1
EurPS	Erythromycin	1409019-02	3
Fagron	Erythromycin	16J24-B10-329156	8
fagr	Erythromycin	13A02-N06	1
Fagron	Erythromycin	14/30-B01-300060	3
Fagron	Erythromycin	16J24-B10	4
Fagron	Erythromycin	EBS/1201-008	2
Fagron	Erythromycin	11D13-N09	2
Fagron	Erythromycin	510211362	1
Fagron	Erythromycin	11J06-N05	2
Fagron	Erythromycin	4212E-01362	1
Fagron	Erythromycin	13A02-N06	9
Fagron	Erythromycin	E-250213-2	1
Fagron	Erythromycin	E-030613-1	1
Fagron	Erythromycin	13A02N06	1
Fagron	Erythromycin	13D30-N01	23
Fagron	Erythromycin	13A02-No6	1
Fagron	Erythromycin	13A02-N060571/680	1
Fagron	Erythromycin	13d30-n01	1
Fagron	Erythromycin	13D30-N010336/730	1
Fagron	Erythromycin	13D30-N010278/730	1
Fagron	Erythromycin	13D30N01	1
Fagron	Erythromycin	12E24-No4	1
Fagron	Erythromycin	13A02-N-06	1
Fagron	Erythromycin	EB078B13	1
Fagron	Erythromycin	13H22-N07	7
Fagron	Erythromycin	14B06-B35	11

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Erythromycin	14B06-B35-290875	8
Fagron	Erythromycin	14B06-35-290873	1
Fagron	Erythromycin	14B06-B35-293509	6
Fagron	Erythromycin	13175602	1
Fagron	Erythromycin	14F13-B02-293488	3
Fagron	Erythromycin	13175803	1
Fagron	Erythromycin	14b06-b35-293509	1
Fagron	Erythromycin	14F13-B02-293490	2
Fagron	Erythromycin	14F13-B02	2
Fagron	Erythromycin	13175810	1
Fagron	Erythromycin	14F13-B02-293487	1
Fagron	Erythromycin	14I30-B01-300062	3
Fagron	Erythromycin	14I30-B01-300060	2
Fagron	Erythromycin	14i30b01-300059	1
Fagron	Erythromycin	14I30B01	1
Fagron	Erythromycin	14I30-B01-300063	1
Fagron	Erythromycin	14/30B0130050	1
Fagron	Erythromycin	14I30-B01-303884	6
Fagron	Erythromycin	1409019-02	5
Fagron	Erythromycin	1430B01303884	1
Fagron	Erythromycin	14/30-B01	1
Fagron	Erythromycin	14I30-B01-300050	2
Fagron	Erythromycin	EB068/14	1
Fagron	Erythromycin	14i30-b01-303884	1
Fagron	Erythromycin	1430-B01-308789	1
Fagron	Erythromycin	14/30-B01_308790	1
Fagron	Erythromycin	14I30-B01-308188	4
Fagron	Erythromycin	14I30-B01-308789	1
Fagron	Erythromycin	14/30-B01-308189	2
Fagron	Erythromycin	14i30-b01-311166	1
Fagron	Erythromycin	16G06-B03-324463	11
Fagron	Erythromycin	16G06-B03-324465	6
Fagron	Erythromycin	16079208	1
Fagron	Erythromycin	16G06-B03324464	1
Fagron	Erythromycin	16G06-B03-329157	5
Fagron	Erythromycin	16g06-b03-329150	1
Fagron	Erythromycin	16079608	1
Fagron	Erythromycin	16J24-B10-3367363	1
Fagron	Erythromycin	16J24-b10-329155	1
Fagron	Erythromycin	16J24-B10-336735	5
Fagron	Erythromycin	1705038-01	3
Fagron	Erythromycin	16J24-B10-346206	4
Fagron	Erythromycin	18F05-B01-350907	3
Fagron	Erythromycin	18F05-B01-350908	3
Fagron	Erythromycin	18F05-B01-352501	3
Fagron	Erythromycin	18F05-B01-353586	4
Fagron	Erythromycin	18f05-b01-350908	1
Fagron	Erythromycin	18f05-b01-352501	1
Fagron	Erythromycin	18F05-B01-352500	4
Fagron	Erythromycin	18f05-b01-353586	1
Fagron	Erythromycin	18F05-B01-353587	2
Fagron	Erythromycin	18F05-B01-356705	1
Fagron	Erythromycin	cepb001e18	1
Fagron	Erythromycin	18096205	1
Fagron	Erythromycin	18f01-b0a-353587	1
Fagron	Erythromycin	18F05-B01-358087	1
Fagron	Erythromycin	19C21-B03-361401	2
Fagron	Erythromycin	19C21-B03-361400	2
Fagron	Erythromycin	15G07-B05-312356	2
Fagron	Erythromycin	13f12-n21	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Erythromycin	14b06-b35-290872	1
Fagron	Erythromycin	14F13-B12-300061	1
Fagron	Erythromycin	14B06-B35-290873	4
Fagron	Erythromycin	14B06-B35290873	1
Fagron	Erythromycin	14B06-B35-293508	2
Fagron	Erythromycin	14I30-B01-3000060	1
Fagron	Erythromycin	13D30-N01003/456	1
Fagron	Erythromycin	13H22-N070126/246	1
Fagron	Erythromycin	14F13-B02-293511	3
Fagron	Erythromycin	14F13-B02-300061	3
Fagron	Erythromycin	1430-B01-303884	1
Fagron	Erythromycin	16J24-B10-329158	2
Fagron	Erythromycin	EB06814	1
Fagron	Erythromycin	11J06-No5	1
Fagron	Erythromycin	18F05-B01	4
Fagron	Erythromycin	16J24-B10-339487	8
Fagron	Erythromycin	16J24-B10-341877	1
Fagron	Erythromycin	1430B01300059	1
Fagron	Erythromycin	EB022E14	2
Fagron	Erythromycin	14I30-B01-308189	1
Fagron	Erythromycin	16G06-B03	6
Fagron	Erythromycin	14I30-B01-311166	2
Fagron	Erythromycin	17088402	1
Fagron	Erythromycin	16J24-B10-339488	3
Fagron	Erythromycin	16G06-B03-324464	11
Fagron	Erythromycin	12J30-N01	13
Fagron	Erythromycin	14I30-B01	5
Fagron	Erythromycin	16G06-B03-324466	6
Fagron	Erythromycin	16J24-B10-329154	1
Fagron	Erythromycin	14B06-B35-290866	4
Fagron	Erythromycin	16G06-B03-324462	2
Fagron	Erythromycin	16/24-B10-329158	1
Fagron	Erythromycin	18F05-B01-358088	3
Fagron	Erythromycin	16G06-B03-329150	6
Fagron	Erythromycin	CEPEB001E18	2
Fagron	Erythromycin	1430-b01-300060	1
Fagron	Erythromycin	14F13-B02-296464	3
Fagron	Erythromycin	14/30-B01-308789	3
Fagron	Erythromycin	0EBA/0010516	2
Fagron	Erythromycin	16g06-b03-324463	2
Fagron	Erythromycin	16J24-B10-329155	3
Fagron	Erythromycin	16j24-b10-329158	1
Fagron	Erythromycin	16G06_B03_324466	1
Fagron	Erythromycin	14/30-B01-303884	1
Fagron	Erythromycin	13175503	1
Fagron	Erythromycin	3000-50	1
Fagron	Erythromycin	16G06-B03_0003	1
Fagron	Erythromycin	19C21-B03-361724	1
Fagron	Erythromycin	EB032J13	4
Fagron	Erythromycin	300059	1
Fagron	Erythromycin	1508034-01	2
Fagron	Erythromycin	16G06B03-329149	1
Fagron	Erythromycin	0EBA/0020516	2
Fagron	Erythromycin	16j24-b10	1
Fagron	Erythromycin	16/24-B10-339487	2
Fagron	Erythromycin	16J24-B10-341875	4
Fagron	Erythromycin	16/24-B10-341875	1
Fagron	Erythromycin	17088005	1
Fagron	Erythromycin	18F05-B01-353588	2
Fagron	Erythromycin	18f05-b01	1

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Supplier	Substance	Batch	Spectra
Fagron	Erythromycin	19C21-B03-361402	2
Fagron	Erythromycin	1205036-01	1
Fagron	Erythromycin	14b06b5293508	1
Fagron	Erythromycin	14/30B01300060	1
Fagron	Erythromycin	700770-0002	1
Fagron	Erythromycin	18F-05-B01	1
Fargon/Sanacorp	Erythromycin	16J24-B10-329158	1
Fiebig	Erythromycin	1409019-02	1
Fiebig	Erythromycin	1607038-02	1
Fiebig	Erythromycin	17088005	1
Fiebig05.2021	Erythromycin	1607038-02	1
Finteler Apotheke	Erythromycin	1607038-02	1
Gatt-Koller	Erythromycin	1803029	2
gehe	Erythromycin	1607038-02	2
Gehe	Erythromycin	11D13-N09	1
Gehe	Erythromycin	12E24-N04	1
Gehe	Erythromycin	12152105	1
Gehe	Erythromycin	12152108	1
Gehe	Erythromycin	1106036-05	1
Gehe	Erythromycin	13189001	2
Gehe	Erythromycin	13F12-N21	1
Gehe	Erythromycin	1308016-02	1
Gehe	Erythromycin	1409019-01	3
Gehe	Erythromycin	15042603	1
Gehe	Erythromycin	15042705	1
Gehe	Erythromycin	15245004	1
Gehe	Erythromycin	16079209	1
Gehe	Erythromycin	16079204	1
Gehe	Erythromycin	16G06-B03	1
Gehe	Erythromycin	1607038-02	1
Gehe	Erythromycin	16079510	1
Gehe	Erythromycin	16J24-B10-336735	1
Gehe	Erythromycin	17088204	1
Gehe	Erythromycin	18F05-B01-352501	1
Gehe	Erythromycin	17088210	1
Gehe	Erythromycin	18F05-B01-358088	1
Gehe	Erythromycin	18096202	1
Gehe	Erythromycin	19C21-B03-361400	1
Gehe	Erythromycin	19C21-B03-361401	1
Gehe	Erythromycin	19C21-B03-361725	1
GEHE	Erythromycin	16079208	1
GEHE	Erythromycin	16079213	2
GEHE	Erythromycin	16079512	1
GEHE	Erythromycin	16079609	2
GEHE	Erythromycin	17088008	1
GEHE	Erythromycin	17088203	2
GEHE	Erythromycin	18096210	1
Fagron	Erythromycin	16G06-B03-329149	4
GEHE 21.05.2014	Erythromycin	1308016-01	1
Caelo	Erythromycin	12152104	2
Caelo	Erythromycin	1181116	1
Caelo	Erythromycin	1171116	1
Caelo	Erythromycin	17088013/1250418	1
Caelo	Erythromycin	18096205	7
Euro OTC	Erythromycin	17088005	1
Fagron	Erythromycin	13F12-N21	24
Fagron	Erythromycin	13175608	1
Fagron	Erythromycin	16J25-B10-329155	1
Caelo	Erythromycin	15042705	11
gepepharm GmbH	Erythromycin	13175502	1

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Supplier	Substance	Batch	Spectra
Gutenberg-Apotheke	Erythromycin	13175608	1
Hedinger	Erythromycin	15245002	2
Klenk	Erythromycin	EB068I14	1
Ichthyol-Gesellschaft	Erythromycin	161020E/1607038-01	1
Jenapharm/Phönix	Erythromycin	1607036-01	1
JENNE	Erythromycin	18096202	2
Kehr	Erythromycin	1705038-01	1
Klosterring	Erythromycin	CEPEB001E18	1
Krieger	Erythromycin	16G06-B03-329150	1
Krieger	Erythromycin	16J24-B10-336735	1
Krieger	Erythromycin	16J24-B10-341876	1
Krieger	Erythromycin	3402	1
L12	Erythromycin	18096203	1
Caelo	Erythromycin	16079206	3
L30	Erythromycin	17088208	1
Midas	Erythromycin	16079609	1
Mikrobiell	Erythromycin	1705038-01	1
Noweda	Erythromycin	11195413	1
Noweda	Erythromycin	11195411	2
Noweda	Erythromycin	12152108	2
Noweda	Erythromycin	12E24-N04	1
Noweda	Erythromycin	12152201	1
Noweda	Erythromycin	13175603	2
Noweda	Erythromycin	13175608	1
Noweda	Erythromycin	130801602	2
Noweda	Erythromycin	14044006	1
Noweda	Erythromycin	14044114	1
Noweda	Erythromycin	15245101	1
Noweda	Erythromycin	150803401	1
Noweda	Erythromycin	1607038-02	1
Noweda	Erythromycin	16079606	1
Noweda	Erythromycin	160703801	1
Noweda	Erythromycin	17088003	1
Noweda	Erythromycin	16J24-B10	1
Noweda	Erythromycin	P2019/92	1
Noweda	Erythromycin	18096302	1
Fagron	Erythromycin	13H22-N070228/246	1
Fagron	Erythromycin	14B06-B35-290874	3
Euro OTC	Erythromycin	160703801	5
Noweda 23.08.2019	Erythromycin	1811019-01	1
Caelo	Erythromycin	12156202	7
Caelo	Erythromycin	14B06-B35-290872	1
Noweda/Euro	Erythromycin	1607038-01	2
Fagron	Erythromycin	14I30B01308189	1
Noweda/Gehe	Erythromycin	14B06-B35-293508	1
Noweda21.04.2015	Erythromycin	14044110	1
Euro OTC	Erythromycin	140901901	3
Euro OTC	Erythromycin	140919-02	1
Euro OTC	Erythromycin	1205036-01	7
OTG/Gehe	Erythromycin	1409019-01	1
Phoenix	Erythromycin	12152201	2
Phoenix	Erythromycin	13175608	1
Phoenix	Erythromycin	14044106	1
Phoenix	Erythromycin	15042609	1
Phoenix	Erythromycin	15042811	1
Phoenix	Erythromycin	16079501	1
Phoenix	Erythromycin	3104	1
Phoenix	Erythromycin	1705038-01	1
Phoenix	Erythromycin	3207	1
Phoenix	Erythromycin	18096205	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Phoenix	Erythromycin	18096302	1
Phoenix	Erythromycin	18096401	2
Phoenix	Erythromycin	1906032-01	2
PHOENIX 08.05.2014	Erythromycin	13175608	2
PHOENIX 08.05.2014	Erythromycin	13175604	1
Phoenix 10.02.2020	Erythromycin	1906032-01	1
Phoenix 28.11.2018	Erythromycin	17088004	1
Fagron	Erythromycin	19C21-B03	1
Phoenix/Cealo	Erythromycin	17088004/0918E-01362	1
Phonix	Erythromycin	17088005	1
phönix	Erythromycin	15245101	1
phönix	Erythromycin	15042611	1
phönix	Erythromycin	15042813	1
phönix	Erythromycin	16079203	1
Phönix	Erythromycin	121427016	1
Phönix	Erythromycin	1205036-02	1
Phönix	Erythromycin	14B06-B35	1
Phönix	Erythromycin	14044201	1
Phönix	Erythromycin	16079205	1
Phönix	Erythromycin	17088002	1
Phönix	Erythromycin	1705038-01	1
Phönix	Erythromycin	1705038-03	1
Phönix	Erythromycin	17088404	1
Phönix	Erythromycin	1811019-01	3
Phönix WE: 23.09.17 E...	Erythromycin	16079604	1
Fagron	Erythromycin	16j24-b10-329155	1
Caelo	Erythromycin	13189004	5
Phönix WE:30.07.2016 ...	Erythromycin	15245101	1
Euro OTC	Erythromycin	170503803	1
Fagron	Erythromycin	16G06-B03-324463	1
Rondell Apotheke	Erythromycin	15042803	1
Sanacorp	Erythromycin	1106036-04	1
Sanacorp	Erythromycin	12152202	1
Sanacorp	Erythromycin	1205035-02	1
Sanacorp	Erythromycin	12156208	1
Sanacorp	Erythromycin	13H22-N07	1
Sanacorp	Erythromycin	59/AKD51	1
Sanacorp	Erythromycin	60/AKD52	1
Sanacorp	Erythromycin	16J24-B10	2
Sanacorp	Erythromycin	17088002	1
Sanacorp	Erythromycin	17088402	1
Sanacorp	Erythromycin	17088203	2
Sanacorp	Erythromycin	1705038-03	1
Sanacorp	Erythromycin	17088302	1
Sanacorp	Erythromycin	181101901	1
Caelo	Erythromycin	11j06-n05	1
Caelo	Erythromycin	59/AKD59	1
Caelo	Erythromycin	60/AKD4	1
Caelo	Erythromycin	160703801	2
Sanacorp;19.03.15;30,50EUR	Erythromycin	1409019-01	1
Caelo	Erythromycin	17088404	17
Caelo	Erythromycin	17088008	9
Spangro _21.05.2019	Erythromycin	1705038-03	1
Caelo	Erythromycin	14044008	4
Unisan	Erythromycin	140901902	1
VDL	Erythromycin	11195407	1
VDL	Erythromycin	160703801	1
Caelo	Erythromycin	11195408	1
Caelo	Erythromycin	12152102	3
Wolff/AHD	Erythromycin	15245004	1

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continued from previous page

Supplier	Substance	Batch	Spectra
	Erythromycin	1308016-02	1
Euro OTC	Erythromycin	1308016-02	26
Caelo	Erythromycin	13175601	10
Caelo	Erythromycin		3
Euro OTC	Erythromycin	1705038	1
Euro OTC	Erythromycin	1508034	1
Euro OTC	Erythromycin	1607038	1
Fagron	Erythromycin	12E24-N04	14
Fagron	Erythromycin	14B06-B35-290872	5
Fagron	Erythromycin		2
Phagron	Erythromycin		1
Sanacorp	Erythromycin		1

- 108 485 spectra from 742 *Apo-Ident* customers from a total of 31 344 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Erythromycin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Erythromycin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	460	0	110 229
Type B	0	440	8	118 694
Type C	0	2742	20	108 485

The substance/substance group *Erythromycin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.9893 %)	98.2143 % (> 97.5446 %)
Type C	100.0000 % (> 99.8899 %)	99.2759 % (> 99.1673 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Erythromycin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol valerate	28.01	—
Dexamethasone	35.54	51.82
Budesonide, micronized	36.13	40.33
Hydrocortisone acetate	38.48	—
Ciclosporin	40.59	—
Triamcinolone acetonide	44.70	33.01
Prednisolon dihydrogen phosphate dinat...	45.54	—
:	:	:
Betamethasone valerate	>50	45.03
Prednicarbate, micronized	>50	60.16
Prednisolone, micronized	>50	70.87
Triamcinolone, micronized	>50	118.66
Capsaicin	>50	161.99
Heparin sodium	>50	169.20
Prednisone	>50	188.71
Betamethasone, micronized	>50	197.60
Norethisterone acetate	>50	219.10

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Erythromycin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24420	24420	0.00	35.72
21669	24420	9.64	37.66
23438	23438	0.00	44.68
21890	21890	0.00	39.12
21323	21890	3.20	40.15
21651	21651	0.00	35.54
22832	22832	0.00	46.36
22438	22438	0.00	38.90
21056	21890	6.85	43.88

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Escin, water-soluble**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20377-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Escin, water-soluble; Aescinum solubile

Special notes

When selecting the *Escin, water-soluble* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Escin, water-soluble	5	3	3

Second-stage model

For differentiation of the substance/substance group *Escin, water-soluble* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Escin, water-soluble*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Escin, water-sol...	1310020-01	21238	40	AR-15-FG-005777-01
Euro OTC	Escin, water-sol...	1506038	21838	60	20150708*
Euro OTC	Escin, water-sol...	1605021	22684	40	20160609*
Fagron	Escin, water-sol...	12K22-N13	21237	40	20121127
Fagron	Escin, water-sol...	12I07-B40-306607	22610	40	1610369

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Escin, water-soluble*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Escin, water-soluble*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Escin, water-soluble	1612012	22988	40
Euro OTC	Escin, water-soluble	1807015-01	24187	40
Euro OTC	Escin, water-soluble	1911023	24939	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Escin, water-soluble*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Escin, water-soluble	1108038	1
Fagron	Escin, water-soluble	30691/M3	1
Euro OTC	Escin, water-soluble	1612012-01	3
Euro OTC	Escin, water-soluble	1310020-01	1

- 111 241 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Escin, water-soluble* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Escin, water-soluble* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	113	7	119 022
Type C	0	3	3	111 241

The substance/substance group *Escin, water-soluble* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	94.1667 % (> 91.6667 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Escin, water-soluble* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	11.73	—
Cyanocobalamin	26.56	—
Glycyrrhizic acid	26.62	—
Nystatin	30.25	—
Methylcobalamin	34.79	—
Calcium citrate tetrahydrate	36.93	—
Ethinylestradiol	39.10	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Escin, water-soluble* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22610	22610	0.00	18.48
21237	21238	2.65	17.51
21238	21238	0.00	14.75
21838	21838	0.00	12.10
22684	22684	0.00	11.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Estradiol benzoate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20098-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Estradiol benzoate; Estradioli benzoas

Special notes

When selecting the *Estradiol benzoate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Estradiol benzoate	6	4	94

Second-stage model

For differentiation of the substance/substance group *Estradiol benzoate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Estradiol benzoate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Estradiol benzoate	15078608	23218	40	20150415
Caelo	Estradiol benzoate	181444	24254	40	20180614*
Euro OTC	Estradiol benzoate	1301006-02	21290	40	1507405
Euro OTC	Estradiol benzoate	1507009	21869	60	0000010566
Euro OTC	Estradiol benzoate	1507009	21869SI	60	0000010566
Fagron	Estradiol benzoate	12H02-N02	20889	40	20120817
Fagron	Estradiol benzoate	12H02-N02	20889SI	60	20120817
Fagron	Estradiol benzoate	14B20-B02	21257	40	20140327
Fagron	Estradiol benzoate	14B20-B02	21257SI	60	20140327

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 9 reference samples from the substance/substance group *Estradiol benzoate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 249 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Estradiol benzoate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Estradiol benzoate	13277607	21324	40
Euro OTC	Estradiol benzoate	1611004	22873	40
Euro OTC	Estradiol benzoate	1412033	24139	40
Euro OTC	Estradiol benzoate	2001032	25113	40
Caelo	Estradiol benzoate	15078608	23218SI [†]	40
Caelo	Estradiol benzoate	181444	24254SI [†]	40
Euro OTC	Estradiol benzoate	1611004	22873SI	40
Euro OTC	Estradiol benzoate	1412033	24139SI	40
Euro OTC	Estradiol benzoate	2001032	25113SI	40

- 118782 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 389 spectra from 263 *Apo-Ident* customers from 102 batches from the substance/substance group *Estradiol benzoate*.
- Among them are spectra of independent samples from 93 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H. 07.06.13 ek: 24,14EUR	Estradiol benzoate	1201019-02	1
Fagron	Estradiol benzoate	17357602	1
AHD	Estradiol benzoate	14B20-B02-292001	1
AHD	Estradiol benzoate	1611004-02	1
AHD	Estradiol benzoate	18144404	1
Euro OTC	Estradiol benzoate	140101-01	1
alliance healthcare 5.12...	Estradiol benzoate	10118576	1
Alliance Healthcare	Estradiol benzoate	1301006-01	1
Bayer Pharma AG / Noweda	Estradiol benzoate	14B20-B02	1
Bayer Pharma/Noweda	Estradiol benzoate	14B20-B02-292001	1
Bayer-Schering	Estradiol benzoate	1007037-03	1
Caelo	Estradiol benzoate	10124918	2
Caelo	Estradiol benzoate	12255904	10
Caelo	Estradiol benzoate	10124909	5
Caelo	Estradiol benzoate	10124919	1
Caelo	Estradiol benzoate	10124912	1
Caelo	Estradiol benzoate	92137389	1
Caelo	Estradiol benzoate	6091305	1
Caelo	Estradiol benzoate	81403700	1
Caelo	Estradiol benzoate	13276401	6

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Estradiol benzoate	13277603	2
Caelo	Estradiol benzoate	21121204	1
Caelo	Estradiol benzoate	13277607	3
Caelo	Estradiol benzoate	1301006-02	1
Caelo	Estradiol benzoate	1201019-02	1
Caelo	Estradiol benzoate	150918EB	1
Caelo	Estradiol benzoate	1507806	1
Caelo	Estradiol benzoate	16003701	5
Caelo	Estradiol benzoate	16003702	3
Caelo	Estradiol benzoate	16003707	13
Caelo	Estradiol benzoate	15078609	1
Caelo	Estradiol benzoate	111004-02	1
Caelo	Estradiol benzoate	181444406	1
Caelo	Estradiol benzoate	181444406	2
Caelo	Estradiol benzoate	181444408	3
Caelo	Estradiol benzoate	15078604	19
Caelo	Estradiol benzoate	15078603	17
Caelo	Estradiol benzoate	12255905	10
Caelo	Estradiol benzoate	15078606	5
Caelo	Estradiol benzoate	10124921	1
Caelo	Estradiol benzoate	181444405	1
Caelo	Estradiol benzoate	13277602	8
Caelo	Estradiol benzoate	15078602	6
Caelo	Estradiol benzoate	1401001-01	1
Caelo	Estradiol benzoate	13277605	3
Caelo	Estradiol benzoate	10124915	2
Caelo	Estradiol benzoate	1149	1
Caelo	Estradiol benzoate	1507009-01	1
Caelo	Estradiol benzoate	181444404	5
Caelo	Estradiol benzoate	17357605	2
Caelo	Estradiol benzoate	eucerin	1
Caelo	Estradiol benzoate	181444405	4
Caelo	Estradiol benzoate	15C10-B04-305523	2
Caelo	Estradiol benzoate	84303830	1
Caesar & Loretz GmbH	Estradiol benzoate	181444402	1
Caesar & Loretz GmbH	Estradiol benzoate	17357605	2
Caesar & Loretz GmbH	Estradiol benzoate	181444405	1
Caesar & Loretz GmbH	Estradiol benzoate	181444406	1
Caesar & Loretz GmbH	Estradiol benzoate	181444408	1
Caesar & Loretz GmbH/An...	Estradiol benzoate	181444404	1
Caesar & Loretz GmbH/Sa...	Estradiol benzoate	181444404	1
Caesar / Gehe	Estradiol benzoate	16003707	1
Caesar&Lorenz / Gehe	Estradiol benzoate	181444405	1
EuRho/Sanacorp	Estradiol benzoate	1201019-02	1
Euro OTC	Estradiol benzoate	1611004-028638831	1
Euro OTC	Estradiol benzoate	1611004-01	7
Euro OTC	Estradiol benzoate	1301006-01	2
Euro OTC	Estradiol benzoate	1201019-02	9
Euro OTC	Estradiol benzoate	121019-01	1
Euro OTC	Estradiol benzoate	1401001-01	10
Euro OTC	Estradiol benzoate	84303830	1
Euro OTC	Estradiol benzoate	1807161	1
Euro OTC	Estradiol benzoate	130100601	1
Euro OTC	Estradiol benzoate	150700901	2
Euro OTC	Estradiol benzoate	1611004-02	4
Euro OTC	Estradiol benzoate	83101340	1
Euro OTC	Estradiol benzoate	14010001-01	1
Euro OTC	Estradiol benzoate	1412033-02	2
EURO Pharma	Estradiol benzoate	84303830	1
Euro OTC	Estradiol benzoate	1007037-02	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Estradiol benzoate	1412033-01	9
Fagron	Estradiol benzoate	17L01-B05-3434714	1
Fagron	Estradiol benzoate	13I11-N01	1
Fagron	Estradiol benzoate	13I11N01	1
Fagron	Estradiol benzoate	81403680	1
Fagron	Estradiol benzoate	13/11-N01	2
Fagron	Estradiol benzoate	81403690	2
Fagron	Estradiol benzoate	13C15-B07-288645	1
Fagron	Estradiol benzoate	11H01-N12	1
Fagron	Estradiol benzoate	15C10-B04-305523	6
Fagron	Estradiol benzoate	1412033-01	1
Fagron	Estradiol benzoate	12B08-N05	1
Fagron	Estradiol benzoate	84303840	1
Fagron	Estradiol benzoate	14B20-B02-292001	6
Fagron	Estradiol benzoate	14B20-B02-2920001	1
Fagron	Estradiol benzoate	14820-B02-294949	1
Fagron	Estradiol benzoate	12L14-N02	1
Fagron	Estradiol benzoate	83101340	2
Fagron	Estradiol benzoate	17L01B05343714	1
Fagron	Estradiol benzoate	17L01-B05-343714	1
Fagron	Estradiol benzoate	15c10-b04-305523	1
Fagron	Estradiol benzoate	11L23-N01	1
Fagron	Estradiol benzoate	2x12L14-N02	1
Fagron	Estradiol benzoate	12D20N06	1
Fagron	Estradiol benzoate	15E08-B08-311705	10
Fagron	Estradiol benzoate	14B20-B02-294949	3
Fagron	Estradiol benzoate	14b20-b02-294949	1
Fagron	Estradiol benzoate	84303830	1
Fagron	Estradiol benzoate	15E08-B08	1
Finze	Estradiol benzoate	1003040-01	2
Gehe	Estradiol benzoate	11L23-N01	1
Gehe	Estradiol benzoate	15078606	1
Gehe	Estradiol benzoate	18144405	2
GEHE	Estradiol benzoate	15078609	1
Caelo	Estradiol benzoate	1100417	1
Kehr	Estradiol benzoate	18144404	1
Klenk	Estradiol benzoate	8(18144402)	1
Krieger	Estradiol benzoate	3401	1
Nachprüfung	Estradiol benzoate	123456	1
Noweda	Estradiol benzoate	13277603	1
Noweda	Estradiol benzoate	15078608	1
Noweda	Estradiol benzoate	18144402	1
Euro OTC	Estradiol benzoate	8011422	1
Euro OTC	Estradiol benzoate	1507009-01	14
Phoenix	Estradiol benzoate	15078608	1
Phoenix	Estradiol benzoate	18144402	1
Phoenix 1.10.2018	Estradiol benzoate	17357602	1
Phoenix WE:20.11.17 1g/...	Estradiol benzoate	16003702	1
Phoenix/Cealo	Estradiol benzoate	1611004-01	1
phönix	Estradiol benzoate	14B20-B02-294949	1
Phönix	Estradiol benzoate	16003707	2
Caelo	Estradiol benzoate	18144402	11
Caelo	Estradiol benzoate	15C10B04305523	1
Caelo	Estradiol benzoate	17357602	5
Euro OTC	Estradiol benzoate	161100402	1
sanacorp	Estradiol benzoate	15078604	1
Sanacorp	Estradiol benzoate	10/AKD24	1
Fagron	Estradiol benzoate	12H02-N052	1
Euro OTC	Estradiol benzoate	1201019-01	7
VDL	Estradiol benzoate	1507009-01	1

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Supplier	Substance	Batch	Spectra
WE:Phönix 21.09.2012	Estradiol benzoate	12B08-N05	1
Caelo	Estradiol benzoate		4
Caelo	Estradiol benzoate	15078608	15
Euro OTC	Estradiol benzoate	1301006-02	10
Fagron	Estradiol benzoate	12H02-N02	3
Fagron	Estradiol benzoate	14B20-B02	3
VDI 16.10.14 12,70 euro	Estradiol benzoate		1

- 110 858 spectra from 742 *Apo-Ident* customers from a total of 31 792 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Estradiol benzoate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Estradiol benzoate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	110 249
Type B	0	360	0	118 782
Type C	0	360	29	110 858

The substance/substance group *Estradiol benzoate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8899 %)	92.5450 % (> 91.7738 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Estradiol benzoate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tetracaine hydrochloride	48.30	—
Ketamine hydrochloride	69.46	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Estradiol benzoate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21257	21290	1.73	86.28
21290	21290	0.00	84.09
24254	24254	0.00	83.76
20889	21290	2.29	87.55
21869	21869	0.00	78.85
23218	21869	7.87	91.46

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Estradiol hemihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20497-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Estradiol hemihydrate; Estradiolum hemihydricum

Special notes

When selecting the *Estradiol hemihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Estradiol hemihydrate	9	18	77

Second-stage model

For differentiation of the substance/substance group *Estradiol hemihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Estradiol hemihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Estradiol hemihy...	12268016	21302	40	1410502
Caelo	Estradiol hemihy...	13285802	21499	60	20130913
Caelo	Estradiol hemihy...	13285802	21500	60	1510622
Caelo	Estradiol hemihy...	13285802	21501	20	20130913
Caelo	Estradiol hemihy...	13285802	21502	20	20130913
Caelo	Estradiol hemihy...	13285802	21503	20	20130913
Caelo	Estradiol hemihy...	13285802	21504	20	20130913
Caelo	Estradiol hemihy...	13285802	21505	20	20130913
Caelo	Estradiol hemihy...	13285802	21506	20	20130913
Caelo	Estradiol hemihy...	13285802	21507	20	20130913
Caelo	Estradiol hemihy...	13285802	21508	60	1410504
Euro OTC	Estradiol hemihy...	1208022-01	21291	40	20121012
Euro OTC	Estradiol hemihy...	1507013	21847	60	1510623
Euro OTC	Estradiol hemihy...	1507013	21847SI	60	1510623
Euro OTC	Estradiol hemihy...	1510039	21945	60	20151103*
Euro OTC	Estradiol hemihy...	1510039	21945SI	89	20151103*
Euro OTC	Estradiol hemihy...	1601017	22307	45	20160122*
Euro OTC	Estradiol hemihy...	1612008	22913	40	20170117*
Euro OTC	Estradiol hemihy...	1612008	22913SI	40	20170117*
Fagron	Estradiol hemihy...	14G24-B04-297404	21667	55	20140825
Fagron	Estradiol hemihy...	16H04-B01-328738	23184	40	20160915

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 889 spectra of 21 reference samples from the substance/substance group *Estradiol hemihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 109 800 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1704 spectra of 46 reference samples from the substance/substance group *Estradiol hemihydrate*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Estradiol hemihydrate	170582	23339	40
Caelo	Estradiol hemihydrate	181443	24257	40
Euro OTC	Estradiol hemihydrate	1607003	22712	40
Euro OTC	Estradiol hemihydrate	1612008-01	23099	40
Euro OTC	Estradiol hemihydrate	1705018	23431	40
Euro OTC	Estradiol hemihydrate	1710031	23779	40
Euro OTC	Estradiol hemihydrate	1802013	24083	40
Euro OTC	Estradiol hemihydrate	1802012	24086	40
Euro OTC	Estradiol hemihydrate	1809022	24319	40
Euro OTC	Estradiol hemihydrate	1808032	24322	40
Euro OTC	Estradiol hemihydrate	1905001	24639	40
Euro OTC	Estradiol hemihydrate	1906013	24772	40
Euro OTC	Estradiol hemihydrate	1910006	24973	40
Euro OTC	Estradiol hemihydrate	1911010	24983	40
Euro OTC	Estradiol hemihydrate	2002008	25108	40
Euro OTC	Estradiol hemihydrate	2002009	25109	40
Euro OTC	Estradiol hemihydrate	2002007	25114	40
Fagron	Estradiol hemihydrate	13K22-N01	21263	40
Caelo	Estradiol hemihydrate	13285802	21499SI [†]	60
Caelo	Estradiol hemihydrate	13285802	21500SI [†]	60
Caelo	Estradiol hemihydrate	13285802	21501SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21502SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21503SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21504SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21505SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21506SI [†]	20
Caelo	Estradiol hemihydrate	13285802	21507SI [†]	20
Caelo	Estradiol hemihydrate	170582	23339SI	30
Caelo	Estradiol hemihydrate	181443	24257SI	40
Euro OTC	Estradiol hemihydrate	1601017	22307SI [†]	45
Euro OTC	Estradiol hemihydrate	1607003	22712SI	40
Euro OTC	Estradiol hemihydrate	1612008-01	23099SI	30
Euro OTC	Estradiol hemihydrate	1705018	23431SI	30
Euro OTC	Estradiol hemihydrate	1710031	23779SI	40
Euro OTC	Estradiol hemihydrate	1802013	24083SI	40
Euro OTC	Estradiol hemihydrate	1802012	24086SI	40
Euro OTC	Estradiol hemihydrate	1809022	24319SI	40
Euro OTC	Estradiol hemihydrate	1808032	24322SI	40
Euro OTC	Estradiol hemihydrate	1905001	24639SI	40
Euro OTC	Estradiol hemihydrate	1906013	24772SI	39
Euro OTC	Estradiol hemihydrate	1910006	24973SI	40
Euro OTC	Estradiol hemihydrate	1911010	24983SI	40

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Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Estradiol hemihydrate	2002008	25108SI	40
Euro OTC	Estradiol hemihydrate	2002009	25109SI	40
Euro OTC	Estradiol hemihydrate	2002007	25114SI	40
Fagron	Estradiol hemihydrate	16H04-B01-328738	23184SI [†]	30

- 117438 spectra from a total of 2399 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 232 spectra from 110 *Apo-Ident* customers from 83 batches from the substance/substance group *Estradiol hemihydrate*.
- Among them are spectra of independent samples from 77 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Estradiol hemihydrate	83100820	2
Anzag; 12.72EUR; 7.10.2015	Estradiol hemihydrate	15038004	1
Bayer Pharma	Estradiol hemihydrate	13K22-N01	2
Bayer Pharma AG	Estradiol hemihydrate	1411024-01	2
Caelo	Estradiol hemihydrate	11078104	1
Caelo	Estradiol hemihydrate	12F29-N03	1
Caelo	Estradiol hemihydrate	22101301	1
Caelo	Estradiol hemihydrate	12268012	4
Caelo	Estradiol hemihydrate	9248916	2
Caelo	Estradiol hemihydrate	13285801	1
Caelo	Estradiol hemihydrate	11078105	1
Caelo	Estradiol hemihydrate	19051501	1
Caelo	Estradiol hemihydrate	15038004	5
Caelo	Estradiol hemihydrate	13285804	1
Caelo	Estradiol hemihydrate	15038014	2
Caelo	Estradiol hemihydrate	15385410	1
Caelo	Estradiol hemihydrate	108082101	1
Caelo	Estradiol hemihydrate	18082105	3
Caelo	Estradiol hemihydrate	13285811	3
Caelo	Estradiol hemihydrate	12268003	1
Caelo	Estradiol hemihydrate	15D01-B02-319032	1
Caelo	Estradiol hemihydrate	18082104	1
Caelo	Estradiol hemihydrate	1705018-01	3
Caelo	Estradiol hemihydrate	12172003	2
Caelo	Estradiol hemihydrate	15385415	1
Caelo	Estradiol hemihydrate	18082101	1
Caelo	Estradiol hemihydrate	15038010	2
Caelo	Estradiol hemihydrate	1503801	1
Caelo	Estradiol hemihydrate	1601017-01	5
Caelo	Estradiol hemihydrate	84201560	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Estradiol hemihydrate	15038016	1
Caelo	Estradiol hemihydrate	15385411	1
Caelo	Estradiol hemihydrate	1612008-01	1
Caesar & Loretz GmbH	Estradiol hemihydrate	18082104	3
Caesar & Loretz GmbH	Estradiol hemihydrate	18082105	1
Caesar & Loretz GmbH	Estradiol hemihydrate	15385415	1
Euro OTC	Estradiol hemihydrate	1612008-01	25
Euro OTC	Estradiol hemihydrate	1612008_01	1
Euro OTC	Estradiol hemihydrate	1705018-01	18
Euro OTC	Estradiol hemihydrate	1808032-01	19
Euro OTC	Estradiol hemihydrate	1607003-0101374814	1
Euro OTC	Estradiol hemihydrate	1504034-01	1
Euro OTC	Estradiol hemihydrate	27061714	1
Euro OTC	Estradiol hemihydrate	1510039-01	1
Euro OTC	Estradiol hemihydrate	15D01-B02	1
Euro OTC	Estradiol hemihydrate	1607003-01	9
Euro OTC	Estradiol hemihydrate	1404030-01	1
Euro OTC	Estradiol hemihydrate	1910006-01	1
Euro OTC	Estradiol hemihydrate	1802013-01	2
Euro OTC	Estradiol hemihydrate	17058205	1
Euro OTC	Estradiol hemihydrate	1308003-01	2
Euro/ Phoenix	Estradiol hemihydrate	3417M-02845	1
Euro OTC	Estradiol hemihydrate	1601017-01	2
Euro OTC	Estradiol hemihydrate	1411024-01	2
Fagron	Estradiol hemihydrate	9G07N01	1
Fagron	Estradiol hemihydrate	13K22-N01	5
Fagron	Estradiol hemihydrate	12F29-N03	6
Fagron	Estradiol hemihydrate	9J27-N05	1
Fagron	Estradiol hemihydrate	12L19-N07	6
Fagron	Estradiol hemihydrate	11H23-N02	1
Fagron	Estradiol hemihydrate	13E07-N02	3
Fagron	Estradiol hemihydrate	12L29-N07	1
Fagron	Estradiol hemihydrate	11031401	1
Fagron	Estradiol hemihydrate	13k22n01	1
Fagron	Estradiol hemihydrate	14G24-B04-297402	3
Fagron	Estradiol hemihydrate	14G24-B04-297406	1
Fagron	Estradiol hemihydrate	14G24-B04-297405	1
Fagron	Estradiol hemihydrate	15D01-B02-308190	1
Fagron	Estradiol hemihydrate	15D01-B02-308568	1
Fagron	Estradiol hemihydrate	15D01-B02-319032	3
Fagron	Estradiol hemihydrate	16h04-b01-328738	1
Fagron	Estradiol hemihydrate	16D12B01326783	1
Fagron	Estradiol hemihydrate	16D12-B01-326783	5
Fagron	Estradiol hemihydrate	16h04-b01-334200	1
Fagron	Estradiol hemihydrate	18F18-B01-351789	1
Fagron	Estradiol hemihydrate	84201560	1
Fagron	Estradiol hemihydrate	16H04-B01-339490	1
Fagron	Estradiol hemihydrate	18F18-B01-351790	1
Fagron	Estradiol hemihydrate	14G24-B04-302446	3
Fagron	Estradiol hemihydrate	13K22N01	1
Fagron	Estradiol hemihydrate	11A21-N01	1
Fagron	Estradiol hemihydrate	84201170	1
Fagron	Estradiol hemihydrate	15D01-B02-312068	2
Fagron	Estradiol hemihydrate	1802013-01	3
Fagron	Estradiol hemihydrate	302446	1
Fagron	Estradiol hemihydrate	16H04-B01-334200	2
Fagron	Estradiol hemihydrate	16h04-b01-337595	1
Fiebig	Estradiol hemihydrate	16H04-B01	1
Gatt-Koller	Estradiol hemihydrate	1801604	2
Gehe	Estradiol hemihydrate	82404160	1

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Supplier	Substance	Batch	Spectra
Gehe	Estradiol hemihydrate	15038016	1
Fagron	Estradiol hemihydrate	18F18-B01-351946	2
Noweda	Estradiol hemihydrate	12268008	1
Noweda	Estradiol hemihydrate	15038004	1
phönix	Estradiol hemihydrate	13285802	1
Sanacorp	Estradiol hemihydrate	15038010	1
Caelo	Estradiol hemihydrate	11078113	1
Caelo	Estradiol hemihydrate	13285802	4
Fagron	Estradiol hemihydrate	14G24-B04-297404	1
Fagron	Estradiol hemihydrate	16H04-B01-328738	1

- 111 015 spectra from 742 *Apo-Ident* customers from a total of 31 808 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Estradiol hemihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Estradiol hemihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	889	0	109 800
Type B	0	1683	21	117 438
Type C	0	229	3	111 015

The substance/substance group *Estradiol hemihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.3251 %)
Type B	100.0000 % (> 99.9893 %)	98.7676 % (> 98.5915 %)
Type C	100.0000 % (> 99.8899 %)	98.7069 % (> 97.4138 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Estradiol hemihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Colistin sulfate	24.25	—
Polymyxin B sulfate	28.99	—
Minoxidil	32.87	—
Nystatin	37.32	—
Bacitracin	39.72	—
Dihydrocodeine hydrogen tartrate	40.81	—
Thiamine chloride hydrochloride	42.61	—
Magnesium citrate	43.11	—
Prednisone	43.14	—
Prednisolon dihydrogen phosphate dinat...	48.59	—
L-glutathione	50.65	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Estradiol hemihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21847	21847	0.00	42.56
21291	21945	2.98	35.33
21667	21945	1.45	32.58
21945	21945	0.00	33.82
22307	22307	0.00	34.99
22913	22913	0.00	30.93
23184	22307	3.47	38.58
21302	21302	0.00	42.43
21499	21847	4.59	41.15
21500	21500	0.00	43.11
21501	21302	4.00	37.94
21502	21302	3.35	37.82
21503	21302	2.32	35.51
21504	21302	4.29	36.79
21505	21302	3.39	34.49
21506	21302	3.70	34.92
21507	21302	3.43	42.50
21508	21508	0.00	45.45

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Estradiol valerate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20330-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Estradiol valerate; Estradioli valeras

Special notes

When selecting the *Estradiol valerate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Estradiol valerate	5	1	81

Second-stage model

For differentiation of the substance/substance group *Estradiol valerate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Estradiol valerate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Estradiol valerate	13264001	21411	60	1410503
Caelo	Estradiol valerate	13264001	21411SI	45	1410503
Caelo	Estradiol valerate	13264001	21416	120	1510624
Caelo	Estradiol valerate	13264001	21416SI	45	1510624
Caelo	Estradiol valerate	13264001	21417	20	20130920
Caelo	Estradiol valerate	13264001	21418	20	20130920
Caelo	Estradiol valerate	13264001	21419	20	20130920
Caelo	Estradiol valerate	13264001	21422	20	20130920
Caelo	Estradiol valerate	13264001	21423	20	20130920
Caelo	Estradiol valerate	13264001	21424	60	1410503
Caelo	Estradiol valerate	13264001	21425	20	20130920
Caelo	Estradiol valerate	13264001	21426	20	20130920
Caelo	Estradiol valerate	15194802	21989	60	20150708
Caelo	Estradiol valerate	15194802	21989SI	30	20150708
Caelo	Estradiol valerate	163277	23056	40	20161221*
Caelo	Estradiol valerate	163277	23056SI	40	20161221*
Fagron	Estradiol valerate	12D18-N02	20651	40	20120426
Fagron	Estradiol valerate	12D18-N02	21266	40	20120118
Fagron	Estradiol valerate	14E26-B02-294846	21646	60	20140616

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 780 spectra of 19 reference samples from the substance/substance group *Estradiol valerate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 109 909 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 187 spectra of 9 reference samples from the substance/substance group *Estradiol valerate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Estradiol valerate	180674	24030	40
Caelo	Estradiol valerate	13264001	21417SI [†]	14
Caelo	Estradiol valerate	13264001	21418SI [†]	15
Caelo	Estradiol valerate	13264001	21419SI [†]	15
Caelo	Estradiol valerate	13264001	21422SI [†]	17
Caelo	Estradiol valerate	13264001	21423SI [†]	15
Caelo	Estradiol valerate	13264001	21425SI [†]	15
Caelo	Estradiol valerate	13264001	21426SI [†]	16
Caelo	Estradiol valerate	180674	24030SI	40

- 118 955 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 195 spectra from 97 *Apo-Ident* customers from 89 batches from the substance/substance group *Estradiol valerate*.
- Among them are spectra of independent samples from 82 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Estradiol valerate	18067413	1
Caelo	Estradiol valerate	18067417	1
Bayer Pharma AG	Estradiol valerate	15C10-B05-305395	1
Bayer Pharma GmbH	Estradiol valerate	82201620	1
Beiersdorf/AHD	Estradiol valerate	12A20-N10	1
Caelo	Estradiol valerate	18067416	3
Caelo	Estradiol valerate	4214U-03259	1
Caelo	Estradiol valerate	15C10B05308851	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Estradiol valerate	15c10-b05-314840	1
Caelo	Estradiol valerate	15C10-B05-321675	1
Caelo	Estradiol valerate	16327706	4
Caelo	Estradiol valerate	15C10-B05	2
Caelo	Estradiol valerate	16327709	5
Caelo	Estradiol valerate	16327710	1
Caelo	Estradiol valerate	1810013	1
Caelo	Estradiol valerate	14E26-B02-294845	1
Caelo	Estradiol valerate	13264002	1
Caelo	Estradiol valerate	15C10-805	1
Caelo	Estradiol valerate	14E26-B02-294844	1
Caelo	Estradiol valerate	18062402	1
Caelo	Estradiol valerate	18067409	3
Caelo	Estradiol valerate	16327711	2
Caelo	Estradiol valerate	5315A-03259	1
Caelo	Estradiol valerate	15C10-B05-314840	1
Caelo	Estradiol valerate	16327703	1
Caelo	Estradiol valerate	18067402	9
Caelo	Estradiol valerate	19061503	2
Caelo	Estradiol valerate	18067407	2
Caelo	Estradiol valerate	test	1
Caelo	Estradiol valerate	15c10-B05-305396	1
Caelo	Estradiol valerate	16F09-B01-332756	1
Caelo	Estradiol valerate	18067412	1
Caelo	Estradiol valerate	19061507	1
Caelo	Estradiol valerate	18067405	1
Caelo	Estradiol valerate	18067403	1
Caelo	Estradiol valerate	18067410	1
Caelo	Estradiol valerate	16327702	5
Caelo	Estradiol valerate	13264003	1
Caelo	Estradiol valerate	15194808	1
Caesar & Loretz GmbH	Estradiol valerate	18067416	1
Euro OTC	Estradiol valerate	1606022-01	1
Euro OTC	Estradiol valerate	15C10-b05	1
Fagron	Estradiol valerate	15C10-B05-318405	1
Fagron	Estradiol valerate	814M-03259	1
Fagron	Estradiol valerate	11K04-N04	1
Fagron	Estradiol valerate	12G05-N09	2
Fagron	Estradiol valerate	12G05N09	1
Fagron	Estradiol valerate	11G18-N04	1
Fagron	Estradiol valerate	13D16N10	1
Fagron	Estradiol valerate	11J13-N09	1
Fagron	Estradiol valerate	13G09N05	1
Fagron	Estradiol valerate	13J13-N02	1
Fagron	Estradiol valerate	13I13-N02	2
Fagron	Estradiol valerate	14E26-B02-294844	1
Fagron	Estradiol valerate	14E26-B02-294847	1
Fagron	Estradiol valerate	14E26-B02-296348	7
Fagron	Estradiol valerate	14E26-B02-294845	3
Fagron	Estradiol valerate	14E26-B02-302873	3
Fagron	Estradiol valerate	14E26B02	2
Fagron	Estradiol valerate	15C10-B05	2
Fagron	Estradiol valerate	15C10-B05-305395	3
Fagron	Estradiol valerate	15C10-B05-321675	7
Fagron	Estradiol valerate	27061710	1
Fagron	Estradiol valerate	16F09-B01	1
Fagron	Estradiol valerate	18G05-B02-353985	3
Fagron	Estradiol valerate	VFM002-1C	1
Fagron	Estradiol valerate	82201620	1
Fagron	Estradiol valerate	19c10-b05-318405	1

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Supplier	Substance	Batch	Spectra
Fagron	Estradiol valerate	15c10-b05-309186	1
Fagron	Estradiol valerate	15C10-B05-313568	1
Fagron	Estradiol valerate	16F09-B01-328135	3
Fagron	Estradiol valerate	13A07-N11	6
Fagron	Estradiol valerate	13G09-N05	5
Fagron	Estradiol valerate	12K05-N02	2
Fagron	Estradiol valerate	16F09B01328135	1
Fagron	Estradiol valerate	15C10-B05-305396	1
Fagron	Estradiol valerate	12A20-N10	2
Fagron	Estradiol valerate	11k04-n04	1
Fagron	Estradiol valerate	24052014a	1
Fagron	Estradiol valerate	15C10-B05-308851	7
Fagron	Estradiol valerate	15C10-B05-309186	3
Fagron	Estradiol valerate	15C10-B05-314840	3
Fagron	Estradiol valerate	15C10-B05-318405	1
Fagron	Estradiol valerate	84404140	3
Fagron	Estradiol valerate	15C10-B05_314840	1
Fagron	Estradiol valerate	11J13-No9	1
Fagron	Estradiol valerate	15c10-b05-314840	1
Fagron	Estradiol valerate	15C10B05321675	1
Fagron	Estradiol valerate	15C10-B05-326087	1
Fagron	Estradiol valerate	15C10B05-326087	1
Fagron	Estradiol valerate	16F09-B01-332756	3
Fagron	Estradiol valerate	18g05-b02	1
Frago/Gehe	Estradiol valerate	15C10-B0508561040	1
Frago/Noweda	Estradiol valerate	16F09-B01-329621	1
Frago/Noweda	Estradiol valerate	16F09-B01	2
Frago/Noweda	Estradiol valerate	16F09-B01-332757	1
Fragon	Estradiol valerate	15C10-B05-5314840	1
GEHE	Estradiol valerate	16F09-B01-332757	1
Fagron	Estradiol valerate	16F09-B01_332756	1
Hedinger/Noweda	Estradiol valerate	15C10-B05	1
Noweda	Estradiol valerate	12A20-N10	1
Fagron	Estradiol valerate	13D16-N10	4
Fagron	Estradiol valerate	13g09-n05	1
Phoenix	Estradiol valerate	13G09-N05	1
Phönix	Estradiol valerate	15C10-B05-326087	1
Sanacorp	Estradiol valerate	13264002	1
THC/Phönix	Estradiol valerate	18067402	1
Caelo	Estradiol valerate	12G05-N09	2
Caelo	Estradiol valerate	13264001	1
Fagron	Estradiol valerate	12D18-N02	3

- 111 052 spectra from 742 *Apo-Ident* customers from a total of 31 804 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Estradiol valerate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Estradiol valerate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	780	0	109 909
Type B	0	187	0	118 955
Type C	0	182	13	111 052

The substance/substance group *Estradiol valerate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.2308 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.7914 %)
Type C	100.0000 % (> 99.8899 %)	93.3333 % (> 91.7949 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Estradiol valerate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methylcellulose	38.15	—
Prednisolon dihydrogen phosphate dinat...	41.79	—
Dexamethasone	43.69	—
Budesonide, micronized	53.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Estradiol valerate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20651	21411	2.58	43.69
21411	21411	0.00	45.24
21417	21416	1.26	46.18
21418	21416	4.54	48.26
21419	21416	1.01	46.15
21422	21416	2.72	47.80

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21423	21416	1.84	45.98
21425	21416	1.22	47.09
21426	21416	1.08	47.06
21266	21416	3.88	48.19
21424	21424	0.00	46.16
21646	21416	3.39	47.79
23056	23056	0.00	50.10
21416	21416	0.00	46.58
21989	21416	1.85	47.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Estriol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20878-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Estriol; Estriolum

Special notes

When selecting the *Estriol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Estriol	8	9	116

Second-stage model

For differentiation of the substance/substance group *Estriol* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Estriol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Estriol	12298706	20878	40	20121106
Caelo	Estriol	13256001	21390	55	1511155
Caelo	Estriol	13256001	21390SI	60	1511155
Caelo	Estriol	13256001	21391	60	20130821
Caelo	Estriol	13256001	21392	20	20130821
Caelo	Estriol	13256001	21393	60	20130821
Caelo	Estriol	13256001	21394	20	20130821
Caelo	Estriol	13256001	21395	20	20130821
Caelo	Estriol	13256001	21399	20	20130821
Caelo	Estriol	13256001	21400	20	20130821
Caelo	Estriol	13256001	21401	20	20130821
Caelo	Estriol	13256001	21404	20	20130821
Euro OTC	Estriol	1507026	21848	60	0000010671
Euro OTC	Estriol	1507026	21848SI	60	0000010671
Euro OTC	Estriol	1509042	21939	60	20151009*
Euro OTC	Estriol	1509042	21939SI	60	20151009*
Euro OTC	Estriol	1703044	23181	40	20170502*
Fagron	Estriol	11J13-N07	21255	40	1412180
Fagron	Estriol	16D15-B03-322957	22889	40	20160711
Fagron	Estriol	16D15-B03-322957	22889SI	40	20160711
Fagron	Estriol	16I19-B01-331468	23172	40	20170301

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 855 spectra of 21 reference samples from the substance/substance group *Estriol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 109 834 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 950 spectra of 27 reference samples from the substance/substance group *Estriol*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Estriol	161382	22633	40
Euro OTC	Estriol	1310002-01	21292	40
Euro OTC	Estriol	1606044	22711	40
Euro OTC	Estriol	1610035	22850	40
Euro OTC	Estriol	1710022	23731	40
Euro OTC	Estriol	1710030	23733	40
Euro OTC	Estriol	1803011	24073	40
Euro OTC	Estriol	1903035	24604	40
Euro OTC	Estriol	2002010	25107	40
Caelo	Estriol	13256001	21391SI [†]	60
Caelo	Estriol	13256001	21392SI [†]	20
Caelo	Estriol	13256001	21394SI [†]	20
Caelo	Estriol	13256001	21395SI [†]	20
Caelo	Estriol	13256001	21399SI [†]	20
Caelo	Estriol	13256001	21400SI [†]	20
Caelo	Estriol	13256001	21401SI [†]	20
Caelo	Estriol	13256001	21404SI [†]	20
Caelo	Estriol	161382	22633SI	40
Euro OTC	Estriol	1606044	22711SI	40
Euro OTC	Estriol	1610035	22850SI	40
Euro OTC	Estriol	1703044	23181SI [†]	40
Euro OTC	Estriol	1710022	23731SI	40
Euro OTC	Estriol	1710030	23733SI	40
Euro OTC	Estriol	1803011	24073SI	40
Euro OTC	Estriol	1903035	24604SI	40
Euro OTC	Estriol	2002010	25107SI	40
Fagron	Estriol	16I19-B01-331468	23172SI [†]	30

- 118 192 spectra from a total of 2408 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 327 spectra from 156 *Apo-Ident* customers from 122 batches from the substance/substance group *Estriol*.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- Among them are spectra of independent samples from 111 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Estriol	17133705	2
Caelo	Estriol	17133710	4
Caelo	Estriol	1713373	1
Euro OTC	Estriol	17133706	1
Audor Pharma	Estriol	APL00036940E	2
Audor Pharma	Estriol	APL000036940E	1
Audor Pharma	Estriol	APL00037293E	1
Audor Pharma	Estriol	APL00037293	1
Audor Pharma	Estriol	AP20780041020218E	2
Bayer Pharma GmbH / Phö...	Estriol	15297804	1
Bombastus	Estriol	5128	1
Caelo	Estriol	15028904	7
Caelo	Estriol	11254410	1
Caelo	Estriol	11254402	1
Caelo	Estriol	12032503	4
Caelo	Estriol	10053206	1
Caelo	Estriol	11254412	1
Caelo	Estriol	12H06-N02	1
Caelo	Estriol	12298704	6
Caelo	Estriol	12298702	2
Caelo	Estriol	27061303	1
Caelo	Estriol	17042014B	1
Caelo	Estriol	14077901	1
Caelo	Estriol	14077904	9
Caelo	Estriol	14272101	3
Caelo	Estriol	1477904	1
Caelo	Estriol	24031501	1
Caelo	Estriol	15297804	11
Caelo	Estriol	15028905	1
Caelo	Estriol	15297805	1
Caelo	Estriol	16053404	1
Caelo	Estriol	17133703	2
Caelo	Estriol	18041811	1
Caelo	Estriol	9071801	1
Caelo	Estriol	17348706	4
Caelo	Estriol	18247101	2
Caelo	Estriol	15008902	1
Caelo	Estriol	12032507	5
Caelo	Estriol	16138204	4
Caelo	Estriol	1733706	1
Caelo	Estriol	17348702	6
Caelo	Estriol	16053405	2
Caelo	Estriol	13256004	9
Caelo	Estriol	16317701	5
Caelo	Estriol	12H06N02	1
Caelo	Estriol	14272104	4
Caelo	Estriol	17133704	9
Caelo	Estriol	16/19-B01-331467	1
Caelo	Estriol	12032504	2
Caelo	Estriol	16053409	1
Caelo	Estriol	19035607	2
Caelo	Estriol	14j20-b07	1
Caelo	Estriol	12298707	2
Caelo	Estriol	10H30-N06	1
Caelo	Estriol	1409018-01	1
Caelo	Estriol	15028901	4
Caelo	Estriol	17133706	17

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Supplier	Substance	Batch	Spectra
Caelo	Estriol	17133711	2
Caelo	Estriol	17348707	3
Caelo	Estriol	19035606	1
Caelo	Estriol	1710030-01	2
Caelo	Estriol	17133709	6
Caesar & Loretz GmbH	Estriol	15028901	1
Caesar & Loretz GmbH	Estriol	15028904	1
Caesar & Loretz GmbH	Estriol	19035609	1
Caesar § Lorenz GmbH	Estriol	12298712	1
Caesar&Loretz,AHC, 19.0...	Estriol	15297804	1
Cealo/ Sanacorp	Estriol	17133706	2
Cealo/GEHE	Estriol	17348702	1
Ensbona/ Sanacorp	Estriol	16053405	1
EuRho	Estriol	1710030-01	1
Euro OTC	Estriol	1310002-01	1
Euro OTC	Estriol	1610035-01	5
Euro OTC	Estriol	1703044-01	1
Euro OTC	Estriol	1710030-01	2
Euro OTC	Estriol	170344-01	1
Euro OTC	Estriol	1803011-01	1
Euro OTC	Estriol	15028904	1
Euro OTC	Estriol	1201020-01	1
Euro OTC	Estriol	1409018-01	1
Euro OTC	Estriol	1606044-01	12
Euro/Phönix	Estriol	1509042-01	1
Fagron	Estriol	12F08-N06	1
Fagron	Estriol	12H06-N02	5
Fagron	Estriol	11D13-N11	1
Fagron	Estriol	12A26-N02	2
Fagron	Estriol	12K07-N15	2
Fagron	Estriol	13C15-N04	4
Fagron	Estriol	81100490	1
Fagron	Estriol	13D19-N02	1
Fagron	Estriol	13H28-N01	4
Fagron	Estriol	14B06-B11-291565	1
Fagron	Estriol	14B06-B11-294565	1
Fagron	Estriol	14b06b11291565	1
Fagron	Estriol	14E13-B01-294033	1
Fagron	Estriol	15297804	2
Fagron	Estriol	15A15-B07-312064	1
Fagron	Estriol	15A15-B07-314241	2
Fagron	Estriol	16D15-B03-323017	1
Fagron	Estriol	16I19-B01	1
Fagron	Estriol	16I9-B01	1
Fagron	Estriol	16I19-B01-331467	1
Fagron	Estriol	16/19-B01-351346	1
Fagron	Estriol	16I19-B01-351346	1
Fagron	Estriol	14E13-B01-294034	3
Fagron	Estriol	16I19-B01-332862	1
Fagron	Estriol	16/19-B01-332862	1
Fagron	Estriol	12H06-No2	2
Fagron	Estriol	16D15-B03-323016	2
Fagron	Estriol	16/19-B01-340536	2
Fagron	Estriol	14B06-B11-291563	1
Fagron	Estriol	86200800	1
fargon	Estriol	12a26-n02	1
Fiebig	Estriol	17133711	1
Fischar/Gehe	Estriol	14H29-B02-298072	3
Gehe	Estriol	16053405	1
Gehe 30.12.14	Estriol	14B06-B11-291563	1

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Supplier	Substance	Batch	Spectra
Caelo	Estriol	17348701	12
Haihang Industry	Estriol	20130824	1
Kehr	Estriol	17133704	1
Kehr	Estriol	18247101	1
Kehr/Apomix	Estriol	14077904	1
Noweda	Estriol	11J13-No7	1
Noweda	Estriol	12032504	1
Noweda 19.05.2015	Estriol	14272104	1
Caelo	Estriol	14077903	2
Caelo	Estriol	16317703	4
NWM CHina	Estriol	ES150304	1
Euro OTC	Estriol	1403011-01	2
Phoenix	Estriol	3032	1
Phoenix	Estriol	17348701	1
Phönix /euro	Estriol	1803011-01	1
Caelo	Estriol	16053408	4
Caelo	Estriol	16317702	5
Sanacorp	Estriol	13256004	1
Sanacorp	Estriol	16317701	1
Sanacorp	Estriol	16317702	1
Shandong Northwest Manu...	Estriol	ETL160302	1
Shandong Northwest Manu...	Estriol	ETL160419	1
VDL	Estriol	13256004	1
Audor Pharma	Estriol		5
Aufor/AHD	Estriol		1
Caelo	Estriol	13256001	1
Caelo	Estriol	12298706	1
Fagron	Estriol	11J13-N07	3
Fagron	Estriol	16I19-B01-331468	1
Fagron	Estriol		1

- 110 920 spectra from 742 *Apo-Ident* customers from a total of 31 771 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Estriol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Estriol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	855	0	109 834
Type B	0	950	0	118 192
Type C	0	326	1	110 920

The substance/substance group *Estriol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.2982 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.3684 %)
Type C	100.0000 % (> 99.8899 %)	99.6942 % (> 98.7768 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Estriol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Alfatradiol	39.21	127.90
L-glutathione	45.81	—
Dihydrocodeine hydrogen tartrate	49.67	—
⋮	⋮	⋮
Pregnenolone	>50	191.73
Quinine hydrochloride	>50	199.04
Progesterone, micronized	>50	217.14
Quinine sulfate	>50	231.02
Spirolactone	>50	250.43
Testosterone propionate	>50	310.35

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Estriol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21399	21939	1.96	41.16
21390	21390	0.00	50.76
21848	21848	0.00	45.55
21404	21255	2.18	42.15
21392	21848	4.05	39.85
21939	21939	0.00	39.21
21255	21255	0.00	40.09
21401	21848	2.23	47.45
23172	21939	2.07	40.55
21393	21848	1.22	44.93
22889	23181	2.09	40.94
21395	21390	1.51	48.99

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21394	21848	3.98	39.94
20878	21939	2.45	41.33
23181	23181	0.00	39.64
21391	21390	3.12	47.85
21400	21939	2.00	41.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ethacridine lactate monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20750-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ethacridine lactate monohydrate; Ethacridini lactas monohydricus

Special notes

When selecting the *Ethacridine lactate monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ethacridine lactate monohydrate	6	2	65

Second-stage model

For differentiation of the substance/substance group *Ethacridine lactate monohydrate* the following second-stage model is used:

- [Submodel 9](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ethacridine lactate monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ethacridine lact...	12149507	20750	40	20120619
Caelo	Ethacridine lact...	16273403	23247	40	20161122
Euro OTC	Ethacridine lact...	1206016-02	21636	60	20121019
Euro OTC	Ethacridine lact...	1412034-02	22733	40	20150223
Fagron	Ethacridine lact...	13I24-N03	21265	40	AR-15-FG-007011-02
Fagron	Ethacridine lact...	15A29-B02-306219	22500	40	20150205

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Ethacridine lactate monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Ethacridine lactate monohydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ethacridine lactate monohydr...	172476	23671	40
Caelo	Ethacridine lactate monohydr...	183146	24355	40
Caelo	Ethacridine lactate monohydr...	172476	23798	40

- 119022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 240 spectra from 150 *Apo-Ident* customers from 72 batches from the substance/substance group *Ethacridine lactate monohydrate*.
- Among them are spectra of independent samples from 65 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Ethacridine lactate monohydr...	12324N03	1
AHL	Ethacridine lactate monohydr...	141101	1
Alliance Healthcare	Ethacridine lactate monohydr...	141234-04	1
Anzag	Ethacridine lactate monohydr...	111201	1
Caelo	Ethacridine lactate monohydr...	11J07-N05	1
Bombastus	Ethacridine lactate monohydr...	14A15-B04-300493	1
Bombastus	Ethacridine lactate monohydr...	13/24-N03	1
Caelo	Ethacridine lactate monohydr...	1206016-03	1
Caelo	Ethacridine lactate monohydr...	1412034-01	1
Caelo	Ethacridine lactate monohydr...	15438003	4
Caelo	Ethacridine lactate monohydr...	15438007	4
Caelo	Ethacridine lactate monohydr...	16272401	1
Caelo	Ethacridine lactate monohydr...	1412034-02	1
Caelo	Ethacridine lactate monohydr...	16272406	1
Caelo	Ethacridine lactate monohydr...	1627412	1
Caelo	Ethacridine lactate monohydr...	17247605	12
Caelo	Ethacridine lactate monohydr...	7247805	1
Caelo	Ethacridine lactate monohydr...	1412034-04	2
Caelo	Ethacridine lactate monohydr...	17332312	1
Caelo	Ethacridine lactate monohydr...	18314601	5
Caelo	Ethacridine lactate monohydr...	10288702	1
Caelo	Ethacridine lactate monohydr...	15177608	2
Caelo	Ethacridine lactate monohydr...	12268407	3
Caelo	Ethacridine lactate monohydr...	17247606	1
Caelo	Ethacridine lactate monohydr...	12G02-N13	2
Caelo	Ethacridine lactate monohydr...	17332303	4
Caelo	Ethacridine lactate monohydr...	15177612	1
Caelo	Ethacridine lactate monohydr...	17332316	3
Caelo	Ethacridine lactate monohydr...	16273411	9
Caelo	Ethacridine lactate monohydr...	141203404	1
Caelo	Ethacridine lactate monohydr...	16272410	2
Caelo	Ethacridine lactate monohydr...	15177603	4
Caelo	Ethacridine lactate monohydr...	16272408	3
Caelo	Ethacridine lactate monohydr...	1412034-03	2
Caelo	Ethacridine lactate monohydr...	141203401	1

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Supplier	Substance	Batch	Spectra
Caelo	Ethacridine lactate monohydr...	15/214/R	1
Caelo	Ethacridine lactate monohydr...	15438009	2
Caelo	Ethacridine lactate monohydr...	17332304	11
Caelo	Ethacridine lactate monohydr...	17332314	6
Caelo	Ethacridine lactate monohydr...	162734	1
Caesar & Loretz GmbH	Ethacridine lactate monohydr...	17332314	1
Caesar & Loretz GmbH / ...	Ethacridine lactate monohydr...	18314601	1
Caesar & Loretz GmbH / ...	Ethacridine lactate monohydr...	17332304	1
Caesar & Loretz GmbH / ...	Ethacridine lactate monohydr...	17332314	1
Caesar & Loretz GmbH/An...	Ethacridine lactate monohydr...	17332316	1
Caesar & Loretz GmbH/Gö...	Ethacridine lactate monohydr...	18314607	1
Chinosol/Anzag	Ethacridine lactate monohydr...	2112A-02196	1
Chinosol/Anzag	Ethacridine lactate monohydr...	914E-02196	1
Dermapharm	Ethacridine lactate monohydr...	130201	8
Dermapharm	Ethacridine lactate monohydr...	111201	5
Dermapharm	Ethacridine lactate monohydr...	100201	1
Dermapharm	Ethacridine lactate monohydr...	141101	8
Dermopharm	Ethacridine lactate monohydr...	130201	1
Dermopharm	Ethacridine lactate monohydr...	141101	1
E Plus	Ethacridine lactate monohydr...	17332314	1
Ebert & Jacobi 19.07...	Ethacridine lactate monohydr...	141101	2
Euro OTC	Ethacridine lactate monohydr...	1412034-01	5
Euro OTC	Ethacridine lactate monohydr...	17332304	2
Euro OTC	Ethacridine lactate monohydr...	1412034-03	8
Euro OTC	Ethacridine lactate monohydr...	141203404	1
Euro OTC	Ethacridine lactate monohydr...	1412034-04	1
Euro OTC	Ethacridine lactate monohydr...	2905007v-03	1
Euro OTC	Ethacridine lactate monohydr...	13/24-N03	1
Euro OTC	Ethacridine lactate monohydr...	2905007V-03	1
Euro OTC	Ethacridine lactate monohydr...	A201801002	1
Euro OTC	Ethacridine lactate monohydr...	2905007-01	1
Euro OTC	Ethacridine lactate monohydr...	15438007	1
Euro OTC	Ethacridine lactate monohydr...	1206016-03	6
Euro OTC	Ethacridine lactate monohydr...	1807013-01	2
Fagron	Ethacridine lactate monohydr...	12A02-N10	1
Fagron	Ethacridine lactate monohydr...	12G02-N135-15	1
Fagron	Ethacridine lactate monohydr...	12G02-N13	5
Fagron	Ethacridine lactate monohydr...	12C30-N07	1
Fagron	Ethacridine lactate monohydr...	12J24-N04	1
Fagron	Ethacridine lactate monohydr...	13/24-N03	3
Fagron	Ethacridine lactate monohydr...	14A15-B04-300493	6
Fagron	Ethacridine lactate monohydr...	16e20-b11-322514	1
Fagron	Ethacridine lactate monohydr...	16E20-B11-328430	1
Fagron	Ethacridine lactate monohydr...	1412034-04	1
Fagron	Ethacridine lactate monohydr...	14A15-B04	1
Fagron	Ethacridine lactate monohydr...	16E20-B11-326633	1
Fagron	Ethacridine lactate monohydr...	13/24-N03	1
Fagron	Ethacridine lactate monohydr...	201205001	2
Fagron	Ethacridine lactate monohydr...	12/24-N04	2
Fagron	Ethacridine lactate monohydr...	11/07-N05	1
Fagron	Ethacridine lactate monohydr...	13124-N03	1
Fagron	Ethacridine lactate monohydr...	16E20-B11-322514	5
Finze	Ethacridine lactate monohydr...	90601	1
Gehe	Ethacridine lactate monohydr...	13I24-N03	1
Gehe	Ethacridine lactate monohydr...	141101	1
Gehe	Ethacridine lactate monohydr...	1412034-03	1
Liaoyuang Silver Eagle ...	Ethacridine lactate monohydr...	1412034-02	1
Phoenix	Ethacridine lactate monohydr...	100201	1
phoenix 18.11.2014	Ethacridine lactate monohydr...	13/24-N03	1
Phonix	Ethacridine lactate monohydr...	13I24-N03	1

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Supplier	Substance	Batch	Spectra
Phönix	Ethacridine lactate monohydr...	111201	1
Caelo	Ethacridine lactate monohydr...	18314607	3
Rezepturlager - Verläng...	Ethacridine lactate monohydr...	121/15	1
Rezepturlager - Verläng...	Ethacridine lactate monohydr...	220/17	1
Caelo	Ethacridine lactate monohydr...	16272413	1
Sanacorp HST	Ethacridine lactate monohydr...	17247605	1
Caelo	Ethacridine lactate monohydr...	12149507	3
Caelo	Ethacridine lactate monohydr...	16273403	7
Euro OTC	Ethacridine lactate monohydr...	1412034-02	1
Euro OTC	Ethacridine lactate monohydr...	1206016-02	4
Fagron	Ethacridine lactate monohydr...	13I24-N03	6

- 111 007 spectra from 742 *Apo-Ident* customers from a total of 31 820 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ethacridine lactate monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethacridine lactate monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	234	6	111 007

The substance/substance group *Ethacridine lactate monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	97.5000 % (> 96.2500 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ethacridine lactate monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	17.36	70.66
Oxytetracycline hydrochloride	18.37	—
Sodium cromoglicate	31.51	—
Chloramphenicol	36.46	—
Tosylchloramide sodium	47.48	—
Eosin Y	55.54	—
⋮	⋮	⋮
Vancomycin hydrochloride	>50	145.15
Chlortetracycline hydrochloride	>50	172.15

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ethacridine lactate monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22500	21265	5.62	24.23
20750	21265	4.48	23.85
21265	21265	0.00	24.11
21636	21265	4.37	23.99
22733	21265	7.25	24.27
23247	21265	6.25	24.01

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ethinylestradiol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20950-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ethinylestradiol; Ethinylestradiolum

Special notes

When selecting the *Ethinylestradiol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ethinylestradiol	4	2	9

Second-stage model

For differentiation of the substance/substance group *Ethinylestradiol* the following second-stage model is used:

- [Submodel 4](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ethinylestradiol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ethinylestradiol	13I09-N04	20950	40	1402058
Fagron	Ethinylestradiol	14E15-B03-296049	21705	55	1507109
Fagron	Ethinylestradiol	14E15-B03-296049	21705SI	56	1507109
Fagron	Ethinylestradiol	14E15-B03-310270	21916	60	20140708
Fagron	Ethinylestradiol	14E15-B03-310270	21916SI	60	20140708
Fagron	Ethinylestradiol	14E15-B03-310270	21958	60	20140708
Fagron	Ethinylestradiol	18E25-B01-355721	24584	40	20180810

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 371 spectra of 7 reference samples from the substance/substance group *Ethinylestradiol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 318 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 233 spectra of 6 reference samples from the substance/substance group *Ethinylestradiol*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ethinylestradiol	16B17-B01-329904	23075	40
Fagron	Ethinylestradiol	19J11-F01-367137	25045	40
Fagron	Ethinylestradiol	14E15-B03-310270	21958SI [†]	43
Fagron	Ethinylestradiol	16B17-B01-329904	23075SI	30
Fagron	Ethinylestradiol	18E25-B01-355721	24584SI [†]	40
Fagron	Ethinylestradiol	19J11-F01-367137	25045SI	40

- 118 909 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 11 *Apo-Ident* customers from 11 batches from the substance/substance group *Ethinylestradiol*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Ethinylestradiol	14e15b03296049	1
Fagron	Ethinylestradiol	16B17-B01-333326	1
Fagron	Ethinylestradiol	18E25-B01-353920	1
Fagron	Ethinylestradiol	18E25-B01-351832	2
Fagron	Ethinylestradiol	12D19-N04	1
Fagron	Ethinylestradiol	16B17-B01	1
Fagron	Ethinylestradiol	16B17-B01-320666	1
Fagron	Ethinylestradiol	84100720	1
Fagron	Ethinylestradiol	13G03-N04	1
Fagron	Ethinylestradiol	18E25-B01-355721	1
Fagron	Ethinylestradiol	13I09-N04	1

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ethinylestradiol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethinylestradiol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	False positive	True positive	False negative	True negative
Type A	0	371	0	110 318
Type B	0	214	19	118 909
Type C	0	12	0	111 235

The substance/substance group *Ethinylestradiol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3827 %)
Type B	100.0000 % (> 99.9893 %)	91.8455 % (> 90.5579 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ethinylestradiol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	19.92	109.10
Cyanocobalamin	28.11	167.97
Minoxidil	40.69	—
Triamcinolone, micronized	43.19	—
Escin, water-soluble	44.42	—
Calcium citrate tetrahydrate	46.84	266.03
Methylprednisolone	48.30	—
Methylcobalamin	48.30	338.74
Magnesium citrate	52.90	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ethinylestradiol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21705	21705	0.00	20.78

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20950	20950	0.00	21.00
21916	20950	5.49	19.92
21958	21705	4.41	21.12
24584	20950	10.18	21.58

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ethosuximide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 24100-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ethosuximide; Ethosuximidum

Special notes

When selecting the *Ethosuximide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ethosuximide	2	1	0

Second-stage model

For differentiation of the substance/substance group *Ethosuximide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ethosuximide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Katwijk Chemi...	Ethosuximide	451717	24100	40	20180509
Katwijk Chemi...	Ethosuximide	451645	24101	40	1807457

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 80 spectra of 2 reference samples from the substance/substance group *Ethosuximide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 609 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Ethosuximide*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Katwijk Chemie BV	Ethosuximide	451644	24102	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Ethosuximide*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ethosuximide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethosuximide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	110 609
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Ethosuximide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ethosuximide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol hemihydrate	48.28	—
Lidocaine	51.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ethosuximide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24100	24101	7.50	48.28
24101	24101	0.00	49.28

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ethyl hydrogen fumarate calcium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21532-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ethyl hydrogen fumarate calcium; Calcii ethylhydrogenfumaras

Special notes

When selecting the *Ethyl hydrogen fumarate calcium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ethyl hydrogen fumarate calcium	5	1	1

Second-stage model

For differentiation of the substance/substance group *Ethyl hydrogen fumarate calcium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ethyl hydrogen fumarate calcium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Ethyl hydrogen f...	1310029-01	21562	60	20131126
Euro OTC	Ethyl hydrogen f...	1306012-01	21641	60	1505456
Euro OTC	Ethyl hydrogen f...	1510005	21938	60	20151030*
Euro OTC	Ethyl hydrogen f...	2001042	25132	40	20200331*
Fagron	Ethyl hydrogen f...	13B25-N08	21532	60	1411090

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 5 reference samples from the substance/substance group *Ethyl hydrogen fumarate calcium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 60 spectra of 1 reference samples from the substance/substance group *Ethyl hydrogen fumarate calcium*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Ethyl hydrogen fumarate calc. ...	1601011	22294	60

- 119 082 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 4 *Apo-Ident* customers from 1 batches from the substance/substance group *Ethyl hydrogen fumarate calcium*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Ethyl hydrogen fumarate calc. ...	1510005-01	12

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ethyl hydrogen fumarate calcium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethyl hydrogen fumarate calcium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	60	0	119 082
Type C	0	12	0	111 235

The substance/substance group *Ethyl hydrogen fumarate calcium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ethyl hydrogen fumarate calcium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Doxylamine hydrogen succinate	37.41	—
Griseofulvin	39.38	—
Propyphenazone	42.97	—
Diltiazem hydrochloride	49.90	—
Omeprazole	51.05	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ethyl hydrogen fumarate calcium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21532	21532	0.00	48.15
21562	21641	15.75	70.59
21641	21641	0.00	67.60
21938	21938	0.00	46.60
25132	25132	0.00	46.87

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Fampridine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20902-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fampridine; Fampridinum

Special notes

When selecting the *Fampridine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Fampridine	8	2	21

Second-stage model

For differentiation of the substance/substance group *Fampridine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Fampridine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Fampridine	16276001	22881	40	20161024
Caelo	Fampridine	16276001	22905	40	20161024
Caelo	Fampridine	16276001	23074	40	20161024
Caelo	Fampridine	16276001	23237	40	20161024
Caelo	Fampridine	190675	24724	40	20190506*
Caelo	Fampridine	180219	24756	40	20180214*
Caelo	Fampridine	180219	24756SI	40	20180214*
Fagron	Fampridine	13G26-N06	20902	40	1402686
Fagron	Fampridine	14D11-B06-293750	21541	60	20140113
Fagron	Fampridine	16D11-B07-318220	22491	40	AR-16-FG-011566-01
Fagron	Fampridine	16E25-B03-324097	22894	40	20160609
Fagron	Fampridine	16E25-B03-324097	22945	40	20160609
Fagron	Fampridine	17K20-B02-349165	24439	40	20180103
Fagron	Fampridine	17K20-B02-349165	24439SI	40	20180103

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 580 spectra of 14 reference samples from the substance/substance group *Fampridine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 109 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 195 spectra of 5 reference samples from the substance/substance group *Fampridine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Fampridine	172170	23653	40
Fagron	Fampridine	19G24-B02-363769	24823	40
Caelo	Fampridine	190675	24724SI [†]	40
Fagron	Fampridine	16E25-B03-324097	22894SI [†]	40
Fagron	Fampridine	19G24-B02-363769	24823SI	35

- 118947 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 39 spectra from 13 *Apo-Ident* customers from 23 batches from the substance/substance group *Fampridine*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Fampridine	15350001	1
Caelo	Fampridine	16276002	3
Caelo	Fampridine	17217003	2
Caelo	Fampridine	24111801	1
Caelo	Fampridine	15350002	1
Fagron	Fampridine	13C07-B02-289395	1
Fagron	Fampridine	14D11-B06-296110	1
Fagron	Fampridine	14D11-B40-301641	1
Fagron	Fampridine	14D11-B40-304961	1
Fagron	Fampridine	17D19-B01-333745	1
Fagron	Fampridine	17/19-B01-339467	1
Fagron	Fampridine	16/19-B04-330727	1
Fagron	Fampridine	18121801	1
Fagron	Fampridine	19G24-B02-363768	4
Fagron	Fampridine	19G24-B02-363770	8
Fagron	Fampridine	16D11-B07	1
Fagron	Fampridine	18H01-B08	1

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Fampridine	17/19-B01	2
Fagron	Fampridine	17K20-B02	3
Inresa	Fampridine	220825	1
Noweda	Fampridine	17K20-B02-349165	1
Caelo	Fampridine	19067501	1
Caelo	Fampridine	16276001	1

- 111 208 spectra from 742 *Apo-Ident* customers from a total of 31 868 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Fampridine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fampridine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	580	0	110 109
Type B	0	178	17	118 947
Type C	0	39	0	111 208

The substance/substance group *Fampridine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9655 %)
Type B	100.0000 % (> 99.9893 %)	91.2821 % (> 89.7436 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 84.6154 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fampridine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Phenobarbital	30.49	—
Eosin Y	49.78	—
Sodium cromoglicate	53.85	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Fampridine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24756	24756	0.00	66.00
20902	20902	0.00	64.04
21541	20902	3.71	63.69
22491	22491	0.00	68.23
22881	22491	15.72	65.16
22894	22491	2.13	67.97
22905	22491	15.28	65.20
23074	22491	16.95	65.97
23237	22491	18.98	66.41
24439	22491	6.02	68.32
22945	22491	5.77	66.01
24724	24724	0.00	66.68

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Finasteride (form III)**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20955-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Finasteride (form III); Finasteridum (Form III)

Special notes

When selecting the *Finasteride (form III)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Finasteride (form III)	6	4	14

Second-stage model

For differentiation of the substance/substance group *Finasteride (form III)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Finasteride (form III)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Finasteride (for...	1403016-01	21626	60	1506004
Euro OTC	Finasteride (for...	1403016-02	21750	60	20140505
Euro OTC	Finasteride (for...	1403016-02	21750SI	51	20140505
Euro OTC	Finasteride (for...	1605020	22565	40	20160613*
Euro OTC	Finasteride (for...	1605020	22565SI	40	20160613*
Euro OTC	Finasteride (for...	1610012	22856	40	20161116*
Euro OTC	Finasteride (for...	1610012	22856SI	33	20161116*
Fagron	Finasteride (for...	13I03-N01	20955	40	1411272
Fagron	Finasteride (for...	14A16-B40-295980	21742	60	20140317
Fagron	Finasteride (for...	14A16-B40-295980	21742SI	45	20140317

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 469 spectra of 10 reference samples from the substance/substance group *Finasteride (form III)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 220 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 351 spectra of 9 reference samples from the substance/substance group *Finasteride (form III)*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Finasteride (form III)	1704004	23151	40
Euro OTC	Finasteride (form III)	1804010	24129	40
Euro OTC	Finasteride (form III)	1809019	24342	40
Fagron	Finasteride (form III)	15J15-B02-320084	22594	40
Euro OTC	Finasteride (form III)	1804010	24129SI	40
Euro OTC	Finasteride (form III)	1809019	24342SI	31
Fagron	Finasteride (form III)	15J15-B02-320084	22594SI	40
Fagron	Finasteride (form III)	15J15-B02-320084	22595	40
Fagron	Finasteride (form III)	15J15-B02-320084	22595SI	40

- 118 791 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 25 spectra from 8 *Apo-Ident* customers from 16 batches from the substance/substance group *Finasteride (form III)*.
- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Finasteride (form III)	1809019-01	1
Crystal	Finasteride (form III)	141100801	1
Euro OTC	Finasteride (form III)	1610012-01	2
Euro OTC	Finasteride (form III)	1704004-01	5
Euro OTC	Finasteride (form III)	1809019-01	1
Euro OTC	Finasteride (form III)	1804010-01	2
Euro OTC	Finasteride (form III)	1411008-01	1
Euro OTC	Finasteride (form III)	1605020-01	1
Fagron	Finasteride (form III)	17011303	1
Fagron	Finasteride (form III)	14111305	1
Fagron	Finasteride (form III)	14L23-B02-306981	1
Fagron	Finasteride (form III)	19041707	1
Fagron	Finasteride (form III)	18041810	1
Euro OTC	Finasteride (form III)	C1012/116010	1
Phoenix	Finasteride (form III)	1804010-01	1
Shandong Northwest Manu...	Finasteride (form III)	FNA160604	1
Euro OTC	Finasteride (form III)	1403016-02	1
Fagron	Finasteride (form III)	13I03-N01	2

- 111 222 spectra from 742 *Apo-Ident* customers from a total of 31 875 batches from a further 706

substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Finasteride (form III)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Finasteride (form III)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	469	0	110 220
Type B	0	351	0	118 791
Type C	0	25	0	111 222

The substance/substance group *Finasteride (form III)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7207 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.2906 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 76.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Finasteride (form III)* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dexamethasone acetate	40.14	—
Potassium sorbate	40.45	—
Estradiol hemihydrate	49.46	—
Betamethasone valerate	49.50	—
Estriol	51.23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Finasteride (form III)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20955	20955	0.00	40.14
21742	21626	10.06	53.16
21750	21626	9.68	52.45
21626	21626	0.00	51.23
22565	22565	0.00	51.76
22856	22856	0.00	53.92

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Fluocinolonacetamid, micronized
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	21031-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Fluocinolonacetamid, micronized; Fluocinoloni acetamidum micron.

Special notes

When selecting the *Fluocinolonacetamid, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Fluocinolonacetamid, micronized	5	1	17

Second-stage model

For differentiation of the substance/substance group *Fluocinoloneacetonid, micronized* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Fluocinoloneacetonid, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Fluocinoloneaceto...	12035003	21756	60	20120321
Caelo	Fluocinoloneaceto...	12035003	21756SI	48	20120321
Caelo	Fluocinoloneaceto...	162281	22637	40	20160907*
Caelo	Fluocinoloneaceto...	162281	22637SI	30	20160907*
Euro OTC	Fluocinoloneaceto...	2804013E-01	21031	60	1404008
Euro OTC	Fluocinoloneaceto...	2804013E-01	21077	60	20121206
Euro OTC	Fluocinoloneaceto...	2804013E-01	21822	60	20121206
Euro OTC	Fluocinoloneaceto...	2804013E-01	21822SI	60	20121206
Fagron	Fluocinoloneaceto...	14L19-B04-307101	22267	45	20150219
Fagron	Fluocinoloneaceto...	14L19-B04-307101	22267SI	45	20150219
Fagron	Fluocinoloneaceto...	14L19-B04-307101	23080	40	20150219
Fagron	Fluocinoloneaceto...	17F14-B08-350105	24700	40	20171221

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 588 spectra of 12 reference samples from the substance/substance group *Fluocinoloneacetonid, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 101 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 218 spectra of 6 reference samples from the substance/substance group *Fluocinolonacetomid, micronized*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Fluocinolonacetomid, microni...	172130	23674	40
Caelo	Fluocinolonacetomid, microni...	172130	23674SI	12
Euro OTC	Fluocinolonacetomid, microni...	2804013E-01	21823	60
Euro OTC	Fluocinolonacetomid, microni...	2804013E-01	21823SI	46
Fagron	Fluocinolonacetomid, microni...	14L19-B04-307101	23080SI [†]	20
Fagron	Fluocinolonacetomid, microni...	17F14-B08-350105	24700SI [†]	40

- 118924 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 25 spectra from 16 *Apo-Ident* customers from 19 batches from the substance/substance group *Fluocinolonacetomid, micronized*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Fluocinolonacetomid, microni...	2804013V-03	1
Caelo	Fluocinolonacetomid, microni...	16228108	2
Caelo	Fluocinolonacetomid, microni...	18073203	1
Eurho	Fluocinolonacetomid, microni...	1408022-04	1
Euro OTC	Fluocinolonacetomid, microni...	1408022-02	2
Fagro/Noweda	Fluocinolonacetomid, microni...	15K06-B02-336730	1
Fagron	Fluocinolonacetomid, microni...	13E22-N10	1
Fagron	Fluocinolonacetomid, microni...	13L30B35295489	1
Fagron	Fluocinolonacetomid, microni...	15K06-B02	1
Fagron	Fluocinolonacetomid, microni...	14L19-B04	4
Fagron	Fluocinolonacetomid, microni...	14L19-B04-317248	1
Fagron	Fluocinolonacetomid, microni...	13L30-B35-295489	1
Fagron	Fluocinolonacetomid, microni...	15K06-B02-336730	1
Fagron	Fluocinolonacetomid, microni...	14L19-B04-615699	1
Fargon/Kehr	Fluocinolonacetomid, microni...	14L-19-B04	1
Fargon/Noweda	Fluocinolonacetomid, microni...	13L13-B35	1
Gehe	Fluocinolonacetomid, microni...	18/19-B05	1
Ichthylol Gesellschaft /...	Fluocinolonacetomid, microni...	14L19-B04-321003	1
Caelo	Fluocinolonacetomid, microni...	12035003	1
Euro OTC	Fluocinolonacetomid, microni...	2804013E-01	1

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- 111 222 spectra from 742 *Apo-Ident* customers from a total of 31 872 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Fluocinoloneacetoneid, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fluocinoloneacetoneid, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	588	0	110 101
Type B	0	217	1	118 924
Type C	0	23	2	111 222

The substance/substance group *Fluocinoloneacetoneid, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9796 %)
Type B	100.0000 % (> 99.9893 %)	99.5413 % (> 98.1651 %)
Type C	100.0000 % (> 99.8899 %)	92.0000 % (> 80.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fluocinoloneacetoneid, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	28.13	—
Triamcinolone acetonide	37.92	—
Dexamethasone acetate	38.31	—
Methylprednisolone	44.62	—
Prednisolone, micronized	48.73	—
Betamethasone, micronized	50.23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Fluocinolonacetonid, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21031	21031	0.00	37.92
24700	21031	7.63	39.97
21756	21031	9.08	37.53
21822	21031	11.21	38.19
22267	21031	5.73	40.55
23080	21031	6.20	38.06
21077	21031	1.63	37.99
22637	22637	0.00	47.43

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Folic acid hydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20370-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Folic acid hydrate; Acidum folicum hydricum

Special notes

When selecting the *Folic acid hydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Folic acid hydrate	7	2	10

Second-stage model

For differentiation of the substance/substance group *Folic acid hydrate* the following second-stage model is used:

- [Submodel 7](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Folic acid hydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Folic acid hydrate	1401005-01	21288	40	20140131
Euro OTC	Folic acid hydrate	1508024	21891	60	20150902*
Euro OTC	Folic acid hydrate	1604036	22554	40	20160429*
Euro OTC	Folic acid hydrate	1611009	22868	40	20161201*
Euro OTC	Folic acid hydrate	1911019	25072	40	20191216*
Fagron	Folic acid hydrate	12G17-N05	20767	40	20120727
Fagron	Folic acid hydrate	16C03-B06-322513	23081	40	20160411

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Folic acid hydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 389 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Folic acid hydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Folic acid hydrate	1608030	22818	40
Euro OTC	Folic acid hydrate	1903033	24608	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 17 spectra from 14 *Apo-Ident* customers from 11 batches from the substance/substance group *Folic acid hydrate*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Folic acid hydrate	1604036-01	1
Euro OTC	Folic acid hydrate	1611009-01	4
Euro OTC	Folic acid hydrate	1608030-01	1
Euro OTC	Folic acid hydrate	1611009-02	1
Euro OTC	Folic acid hydrate	1307041-01	1
Fagron	Folic acid hydrate	UT11110182	1
Fagron	Folic acid hydrate	13A11-N01	1
Fagron	Folic acid hydrate	13G16-N02	4
Fagron	Folic acid hydrate	16C03-B06	1
Farmalabor	Folic acid hydrate	P1701610	1
Euro OTC	Folic acid hydrate	1401005-01	1

- 111 230 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Folic acid hydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Folic acid hydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	80	0	119 062
Type C	0	17	0	111 230

The substance/substance group *Folic acid hydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Folic acid hydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bismuth gallath, basic	35.49	162.05
Acetylcysteine	38.73	449.40
Carbomers 35000 / 50000	73.80	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Folic acid hydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20767	22554	3.42	45.20
21288	22554	2.97	44.84
21891	21891	0.00	43.19
22868	22868	0.00	43.95
23081	22554	2.78	44.26
25072	25072	0.00	44.79
22554	22554	0.00	43.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Fructose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20074-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fructose; Fructosum

Special notes

When selecting the *Fructose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Fructose	7	13	193

Second-stage model

For differentiation of the substance/substance group *Fructose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Fructose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Fructose	160667	22481	60	20160425*
Caelo	Fructose	15084311	22490	40	20150316
Euro OTC	Fructose	1212015-01	21281	40	20130111
Euro OTC	Fructose	1509037	21934	60	20151027*
Euro OTC	Fructose	1512009	22292	60	20160113*
Euro OTC	Fructose	1701049	22986	40	20170213*
Fagron	Fructose	16H05-B01-326259	23018	40	20160926
Fagron	Fructose	16H05-B01-326259	23082	40	20160926

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 8 reference samples from the substance/substance group *Fructose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 309 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 561 spectra of 14 reference samples from the substance/substance group *Fructose*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Fructose	15271213	22583	40
Caelo	Fructose	171439	23422	40
Caelo	Fructose	182916	24364	40
Caelo	Fructose	191699	24739	40
Euro OTC	Fructose	1604024	22547	41
Euro OTC	Fructose	1607030	22693	40
Euro OTC	Fructose	1705002	23391	40
Euro OTC	Fructose	1710034	23901	40
Euro OTC	Fructose	1803040	24087	40
Euro OTC	Fructose	1811018	24486	40
Euro OTC	Fructose	1906017	24792	40
Euro OTC	Fructose	1910020	24978	40
Fagron	Fructose	19C19-B02-361846	25057	40
Caelo	Fructose	171439	23673	40

- 118 581 spectra from a total of 2407 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 595 spectra from 147 *Apo-Ident* customers from 197 batches from the substance/substance group *Fructose*.
- Among them are spectra of independent samples from 192 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance health	Fructose	14E01-B04-293505	2
Alliance health	Fructose	14K17-B99-300913	3
Alliance Health 13.02.2...	Fructose	13C25-N03	1
apo-ident	Fructose	1607030-01	2
Beiersdorf	Fructose	14096208	1
Caelo	Fructose	13098915	1
Caelo	Fructose	14096203	1
Caelo	Fructose	130998922	1
Caelo	Fructose	7111401	1
Caelo	Fructose	1081501	1
Caelo	Fructose	1701034-01	1
Caelo	Fructose	10381011	1
Caelo	Fructose	10071201	1
Caelo	Fructose	11071201	1
Caelo	Fructose	11258627	3
Caelo	Fructose	1309213394	1
Caelo	Fructose	11258628	2
Caelo	Fructose	12132305	5
Caelo	Fructose	11258614	1

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Supplier	Substance	Batch	Spectra
Caelo	Fructose	12132309	2
Caelo	Fructose	121e29-n08	1
Caelo	Fructose	12132310	1
Caelo	Fructose	12132314	5
Caelo	Fructose	12H01-N03	1
Caelo	Fructose	7051304	1
Caelo	Fructose	21051303	1
Caelo	Fructose	12132301	2
Caelo	Fructose	12132322	2
Caelo	Fructose	12132313	5
Caelo	Fructose	13098906	4
Caelo	Fructose	13098909	1
Caelo	Fructose	13098914	2
Caelo	Fructose	31031401	1
Caelo	Fructose	13098917	3
Caelo	Fructose	13098918	1
Caelo	Fructose	10051401	1
Caelo	Fructose	13098913	4
Caelo	Fructose	14096201	2
Caelo	Fructose	14096205	3
Caelo	Fructose	20081402	1
Caelo	Fructose	13E27-N07	1
Caelo	Fructose	13098904	1
Caelo	Fructose	18021501	1
Caelo	Fructose	9031504	1
Caelo	Fructose	5061503	1
Caelo	Fructose	14305204	1
Caelo	Fructose	15A16-B07	1
Caelo	Fructose	15A16-B07-305241	1
Caelo	Fructose	1509037-01	2
Caelo	Fructose	152711201	1
Caelo	Fructose	15271201	1
Caelo	Fructose	16066103	3
Caelo	Fructose	16066106	11
Caelo	Fructose	23021708	1
Caelo	Fructose	170104901	1
Caelo	Fructose	17007708	1
Caelo	Fructose	5081701	1
Caelo	Fructose	16283910	3
Caelo	Fructose	13111705	1
Caelo	Fructose	1710034-01	2
Caelo	Fructose	13041802	1
Caelo	Fructose	17143903	1
Caelo	Fructose	9061804	1
Caelo	Fructose	18061801	1
Caelo	Fructose	31101810	1
Caelo	Fructose	18082005	17
Caelo	Fructose	18082012	2
Caelo	Fructose	18291605	2
Caelo	Fructose	17007701	5
Caelo	Fructose	17007707	2
Caelo	Fructose	14096208	2
Caelo	Fructose	18082002	5
Caelo	Fructose	1803040-01	3
Caelo	Fructose	13098911	1
Caelo	Fructose	18291602	8
Caelo	Fructose	11258611	1
Caelo	Fructose	13098902	3
Caelo	Fructose	14096223	5
Caelo	Fructose	15271214	2

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Supplier	Substance	Batch	Spectra
Caelo	Fructose	17007702	1
Caelo	Fructose	13098922	1
Caelo	Fructose	15271208	1
Caelo	Fructose	12132320	1
Caelo	Fructose	18082011	1
Caelo	Fructose	15084312	2
Caelo	Fructose	14096211	1
Caelo	Fructose	14096207	1
Caelo	Fructose	1503045-01	2
Caelo	Fructose	15084305	3
Caelo	Fructose	11107-N06	1
Caelo	Fructose	16066107	8
Caelo	Fructose	12132325	3
Caelo	Fructose	14096219	4
Caelo	Fructose	15A16-B07-308950	2
Caelo	Fructose	18062005	1
Caelo	Fructose	17143904	1
Caelo	Fructose	1610033-01	2
Caelo	Fructose	17346404	19
Caelo	Fructose	13A28-N01	1
Caelo	Fructose	16066101	2
Caelo	Fructose	3313U-03394	1
Caelo	Fructose	15271209	3
Caelo	Fructose	17346411	2
Caelo	Fructose	1114A03394	1
Caelo	Fructose	14096210	1
Caelo	Fructose	14305201	1
Caelo	Fructose	15084301	3
Caelo	Fructose	15084308	2
Caelo	Fructose	14305206	1
Caelo	Fructose	2117E-03394	1
Caelo	Fructose	1714390210087516	1
Caelo	Fructose	17346405	1
Caelo	Fructose	18291612	1
Caelo	Fructose	14305203	2
Caelo	Fructose	14096224	2
Caelo	Fructose	17143902	5
Caelo	Fructose	15271213	6
Caesar & Loretz GmbH	Fructose	16283910	1
Caesar & Loretz GmbH	Fructose	18291602	1
Caesar & Loretz GmbH	Fructose	18307407	1
Caesar & Loretz GmbH / ...	Fructose	18291602	1
Caesar & Loretz GmbH/Ge...	Fructose	18082012	1
Ebert & Jacobi 08.08.16	Fructose	1604024-01	1
EuRho	Fructose	1509037-01	4
EuRho	Fructose	1705002-01	1
EuRho	Fructose	171003401	2
EuRho/Noweda	Fructose	1604024-01	1
Euro OTC	Fructose	2731	1
Euro OTC	Fructose	1205022-01	1
Euro OTC	Fructose	1307022-01	4
Euro OTC	Fructose	1401004-01	4
Euro OTC	Fructose	140100401	1
Euro OTC	Fructose	1503045-01	7
Euro OTC	Fructose	1607030-01	12
Euro OTC	Fructose	AD15190330	1
Euro OTC	Fructose	1701049-01	12
Euro OTC	Fructose	1803040-01	14
Euro OTC	Fructose	180304001	1
Euro OTC	Fructose	1710034-01	23

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Supplier	Substance	Batch	Spectra
Euro OTC	Fructose	171003401	1
Euro OTC	Fructose	1604024-01	3
Euro OTC	Fructose	1803040-012	1
Euro OTC	Fructose	1610033	1
Euro OTC	Fructose	1201017-01	2
Euro OTC	Fructose	1811018-01	15
Euro OTC	Fructose	1509037-01	7
Euro OTC	Fructose	1906017-01	9
Euro OTC	Fructose	1512009-01	8
Euro OTC	Fructose	1610033-01	9
Euro OTC	Fructose	141000901	2
Euro OTC	Fructose	18082002	1
euro//Noweda	Fructose	1509037-01	1
euro//Noweda	Fructose	1710034-01	1
Euro/Gehe	Fructose	1604024-01	1
Euro/Gehe	Fructose	1607030-01	1
Euro/Noweda	Fructose	1610033-01	2
euroct/gehe	Fructose	1212015-01	1
Euro OTC	Fructose	1410009-01	5
Euro OTC	Fructose	1803040-02	1
Euro OTC	Fructose	1705002-01	9
Euro OTC	Fructose	1209010-01	1
Euro OTC	Fructose	121201-01pzn	1
Euro OTC	Fructose	AD16C91215	1
Fagron	Fructose	12A26-N04	1
Fagron	Fructose	508Q-03394	1
Fagron	Fructose	12H01-N03	1
Fagron	Fructose	13J18-B06-286899	1
Fagron	Fructose	13J18-B06-286894	1
Fagron	Fructose	14E01-B04-29350	1
Fagron	Fructose	13E27-n07	1
Fagron	Fructose	14E01-B04	3
Fagron	Fructose	14E01-B04-297098	2
Fagron	Fructose	K43537721	1
Fagron	Fructose	14K17-B99	2
Fagron	Fructose	14K17-B99-300913	1
Fagron	Fructose	14E01B04293506	1
Fagron	Fructose	14E1-B04-293506	1
Fagron	Fructose	15A16-B07	1
Fagron	Fructose	15/21-B01	1
Fagron	Fructose	1521-B01-323021	1
Fagron	Fructose	15121-B01-323021	1
Fagron	Fructose	15I21-B01-323021	5
Fagron	Fructose	15/21-B01-323021	1
Fagron	Fructose	16H05-B01	2
Fagron	Fructose	17007701	1
Fagron	Fructose	18082005	1
Fagron	Fructose	13098906	1
Fagron	Fructose	12H01-N03	1
Fagron	Fructose	1107-N06	1
Fagron	Fructose	14E01-B04-293505	6
Fagron	Fructose	3014Q-03394	1
Fagron	Fructose	516Q-03394	1
Fagron	Fructose	326259	1
Fagron	Fructose	15121-B01-312701	2
Fagron	Fructose	15I21-B01	1
Fagron	Fructose	15/21-B01-312700	1
Fagron	Fructose	FR1413072	1
Fagron	Fructose	FR1443072	8
Fagron	Fructose	13E27-N07	2

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Supplier	Substance	Batch	Spectra
Fagron	Fructose	13C25-N03	3
Fagron	Fructose	1312A-03394	1
Fagron	Fructose	1170	1
Fagron	Fructose	1705002-01	1
Fagron	Fructose	12E29-N08	3
Fagron	Fructose	7K21-N12	1
Fagron	Fructose	14k17-B99	2
Fagron	Fructose	15A16-B07-308950	1
Fagron	Fructose	13A28-N01	10
Fagron	Fructose	12K28-N06	2
Fagron	Fructose	13J18-B06	2
Fagron	Fructose	15A16-B07-305241	1
Fagron	Fructose	15A16-B07-303124	1
Fagron	Fructose	15I21-B01-323020	1
Fagron	Fructose	16H05-B01-330164	2
Fargon	Fructose	15I21-B01-312701	1
Finteler Apotheke	Fructose	16283910	1
fragon	Fructose	FR1413072	1
Gatt Koller	Fructose	1544/05141914	1
Gatt-Koller / Phoenix	Fructose	3156/0813	1
Gehe	Fructose	1607030-01	2
Gehe	Fructose	17346404	1
Gehe	Fructose	18082005	1
Gehe	Fructose	1906017-01	1
GEHE	Fructose	1803040-01	2
GEHE 17.06.2014	Fructose	13098913	1
Euro OTC	Fructose	1803040-1	1
Jenne	Fructose	15A16-B07	1
Jenne	Fructose	14A16-B07	1
JENNE	Fructose	17L22-B02	2
Lihn/Reformhaus	Fructose	713E-03394	2
Noweda	Fructose	1205022-01	1
Noweda	Fructose	16283910	1
Noweda	Fructose	1710034-01	1
Noweda	Fructose	17143902	1
Caelo	Fructose	15271205	5
Caelo	Fructose	1705002-01	1
phoenix	Fructose	1906017-01	1
Phoenix	Fructose	15I21-B01	1
Phoenix	Fructose	1906017-01	1
Phoenix 05.08.2014	Fructose	FR1336122	3
Phoenix 11.12.2018	Fructose	1803040-01	1
Phoenix 17.11.19	Fructose	1803044-01	1
Phoenix 22.12.14	Fructose	1307022-01	1
Phoenix 22.12.14	Fructose	1401004-01	1
Phönix	Fructose	18291602	1
Phönix	Fructose	12K28-N06	1
PHÖNIX	Fructose	1710034-01	1
PHÖNIX	Fructose	17L22-B02-346104	1
Phönix 17.05.2019	Fructose	1811018-01	2
Phönix Euro	Fructose	FS2P00251707-304	1
Caelo	Fructose	15271215	3
Sanacorp	Fructose	K43537721	1
SANACORP	Fructose	1811018-01	2
Caelo	Fructose	12132317	2
Synopharm	Fructose	202A052	1
Caelo	Fructose	15084311	1
Euro OTC	Fructose	1212015-01	2
Fagron	Fructose	16H05-B01-326259	1

- 110 652 spectra from 742 *Apo-Ident* customers from a total of 31 696 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Fructose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fructose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	380	0	110 309
Type B	0	561	0	118 581
Type C	0	595	0	110 652

The substance/substance group *Fructose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.9305 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 98.9916 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fructose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Aciclovir	33.50	—
Potassium sodium tartrate tetrahydrate	36.02	—
Sodium acetate trihydrate	40.46	—
Levothyroxin sodium	45.00	—
Isosorbide dinitrate 40%	47.10	—
Rice starch	48.77	—
SyrSpend® SF Alka	51.38	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Fructose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21281	22292	5.58	29.44
21934	21934	0.00	28.16
22292	22292	0.00	31.03
22481	22481	0.00	30.08
22490	22292	1.75	30.34
22986	22986	0.00	28.94
23018	22292	2.10	30.11
23082	22292	2.78	30.06

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Furosemide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20944-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Furosemide; Furosemidum

Special notes

When selecting the *Furosemide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Furosemide	4	1	18

Second-stage model

For differentiation of the substance/substance group *Furosemide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Furosemide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Furosemide	13A22-N08	20944	40	1401379
Fagron	Furosemide	14K10-B02-301746	21819	60	20141215
Fagron	Furosemide	17D06-B01-338982	23940	40	20170626
Fagron	Furosemide	19I27-F04-366906	25044	40	20191218

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Furosemide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Furosemide*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Furosemide	16B15-B06-322860	23083	40
Fagron	Furosemide	16B15-B06-322860	23084	40

- 119 062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 30 spectra from 24 *Apo-Ident* customers from 22 batches from the substance/substance group *Furosemide*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance Healthcare/Hed...	Furosemide	12/13-N06	1
Caelo	Furosemide	16B15-B06	1
Fagron	Furosemide	12A18-N03	1
Fagron	Furosemide	11K21-N26	1
Fagron	Furosemide	13E28-B40	2
Fagron	Furosemide	13E28-B40-295538	1
Fagron	Furosemide	17D06-B01-335672	2
Fagron	Furosemide	18C27-B02	1
Fagron	Furosemide	16/26-B04-329253	2
Fagron	Furosemide	13E28-B40-289433	1
Fagron	Furosemide	12I13-No6	1
Fagron	Furosemide	AM20216066	1
Fagron	Furosemide	15L10B02316506	1
Fagron	Furosemide	FUR-1A-192016	1
Fagron	Furosemide	17d06-b01-335672	1
Fagron	Furosemide	18C27-B02-348148	2
Fagron	Furosemide	15L10-B02-316506	2
IPCA/Noweda	Furosemide	11D29-N08	1
Fagron	Furosemide	1095H2RI	1
Phoenix	Furosemide	17D06-B01-338982	1
Fagron	Furosemide	13A22-N08	4
Fagron	Furosemide	14K10-B02-301746	1

- 111 217 spectra from 742 *Apo-Ident* customers from a total of 31 870 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Furosemide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Furosemide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	80	0	119 062
Type C	0	30	0	111 217

The substance/substance group *Furosemide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 80.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Furosemide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	55.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Furosemide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20944	20944	0.00	60.84
21819	20944	6.44	60.27
23940	20944	6.42	59.67
25044	20944	2.18	61.46

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Fusidic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20780-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Fusidic acid; Acidum fusidicum

Special notes

When selecting the *Fusidic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Fusidic acid	3	2	22

Second-stage model

For differentiation of the substance/substance group *Fusidic acid* the following second-stage model is used:

- [Submodel 5](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Fusidic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Fusidic acid	12G04-N01	20780	40	1401162
Fagron	Fusidic acid	13L13-B01-289513	21733	60	20140113
Fagron	Fusidic acid	14E01-B08-299791	21897	60	20140605

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Fusidic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Fusidic acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Fusidic acid	15I10-B02-322112	23069	40
Fagron	Fusidic acid	17J06-B02-343675	23943	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 30 spectra from 14 *Apo-Ident* customers from 24 batches from the substance/substance group *Fusidic acid*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Ebert 24.08.16	Fusidic acid	1510-B02_319452	1
Fagron	Fusidic acid	13A07-N10	2
Fagron	Fusidic acid	13L13-B01-289514	1
Fagron	Fusidic acid	13L13-B01	1
Fagron	Fusidic acid	15/10-B02-314192	1
Fagron	Fusidic acid	15I10-B02	1
Fagron	Fusidic acid	1510-B02_319231	1
Fagron	Fusidic acid	15I10B02-319231	1
Fagron	Fusidic acid	15I10-B02-326182	1
Fagron	Fusidic acid	15/10-b02	2
Fagron	Fusidic acid	116E-03682	1
Fagron	Fusidic acid	17G06-B99-337953	1
Fagron	Fusidic acid	17J06-B02-355108	1
Fagron	Fusidic acid	17J06-B02-345542	1
Fagron	Fusidic acid	FS655	1
Fagron	Fusidic acid	17J06-B02-343677	1
Fagron	Fusidic acid	12B23-N03	1
Fagron	Fusidic acid	13H19-N05	1
Fagron	Fusidic acid	4113U-07034	1
Noweda	Fusidic acid	17J06-B02-349947	1
Fagron	Fusidic acid	12G04-No1	1
Phoenix/Cealo	Fusidic acid	701714-0003/0918A-07	1
Fagron	Fusidic acid	14E01-B08-299791	3
Fagron	Fusidic acid	13L13-B01-289513	3

- 111 217 spectra from 742 *Apo-Ident* customers from a total of 31 867 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Fusidic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fusidic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following

table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	80	0	119 062
Type C	0	28	2	111 217

The substance/substance group *Fusidic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	93.3333 % (> 83.3333 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Fusidic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Norethisterone acetate	21.35	—
Estradiol valerate	23.91	—
Budesonide, micronized	24.43	—
Povidone iodine	27.64	95.10
Cannabidiol	50.40	—
⋮	⋮	⋮
Povidone 25, soluble	>50	90.81

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Fusidic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21897	20780	7.71	21.35
21733	20780	2.85	23.70
20780	20780	0.00	22.95

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Galactose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20326-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Galactose; D-Galactopyranose

Special notes

When selecting the *Galactose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Galactose	2	2	24

Second-stage model

For differentiation of the substance/substance group *Galactose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Galactose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Galactose	13I13-B40-287993	21762	60	AR-15-FG-008936-01
Fagron	Galactose	14H05-B09-310972	22259	60	20140818

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 2 reference samples from the substance/substance group *Galactose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 569 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Galactose*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Galactose	11F30-N08	20839	40
Fagron	Galactose	15G13-B04-320810	23106	40
Fagron	Galactose	15G13-B04-320810	23595	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 32 spectra from 3 *Apo-Ident* customers from 25 batches from the substance/substance group *Galactose*.
- Among them are spectra of independent samples from 24 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Galactose	16G22-B01-329906	1
falcento	Galactose	322619PF5	1
Falcento	Galactose	48223PF2	1
Falcento	Galactose	2014	1
Falcento	Galactose	122PF4	1
Falcento	Galactose	1223PF4	3
Falcento	Galactose	2223PF4	3
Falcento	Galactose	5223PF4	3
Falcento	Galactose	222PF4	1
Falcento	Galactose	10440003	1
Falcento	Galactose	13223PF4	1
Falcento	Galactose	233619PF5	1
Falcento	Galactose	92619PF64744/16	1
Falcento	Galactose	82619PF64743/16	1
Falcento	Galactose	82619PF7	1
Falcento	Galactose	72619PF7	1
inalco	Galactose	212619PF5	1
inalco	Galactose	32619PF8	1
inalco	Galactose	42619PF4	1
Phönix	Galactose	39223PF3	1
Phönix	Galactose	12223PF4	2
Unisan	Galactose	432619PF5	1
Unisan	Galactose	382619PF5	1
Unisan	Galactose	442619PF5	1
Phönix 04.03.2014	Galactose		1

- 111 215 spectra from 742 *Apo-Ident* customers from a total of 31 866 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Galactose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Galactose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table

breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	120	0	119 022
Type C	0	32	0	111 215

The substance/substance group *Galactose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 81.2500 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Galactose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	48.20	–
Sodium cromoglicate	50.19	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Galactose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21762	21762	0.00	51.09
22259	21762	5.43	51.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at

least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Gelatine, white**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20206-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gelatine, white; Gelatina alba

Special notes

When selecting the *Gelatine, white* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Gelatine, white	2	2	18

Second-stage model

For differentiation of the substance/substance group *Gelatine, white* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Gelatine, white*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Gelatine, white	11334025	20898	40	20111214
Caelo	Gelatine, white	15320504	22499	40	AR-16-FG-014461-01
Caelo	Gelatine, white	15320504	22582	45	AR-16-FG-011564-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 125 spectra of 3 reference samples from the substance/substance group *Gelatine, white*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 564 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Gelatine, white*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Gelatine, white	172772	23792	40
Caelo	Gelatine, white	154419	23793	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 28 spectra from 19 *Apo-Ident* customers from 19 batches from the substance/substance group *Gelatine, white*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Gelatine, white	4110I-01578	1
Caelo	Gelatine, white	12354401	1
Caelo	Gelatine, white	14130901	2
Caelo	Gelatine, white	15320502	2
Caelo	Gelatine, white	8031701	1
Caelo	Gelatine, white	1544191916	1
Caelo	Gelatine, white	8051811	1
Caelo	Gelatine, white	15441922	1
Caelo	Gelatine, white	17277210	1
Caelo	Gelatine, white	15084806	1
Caelo	Gelatine, white	15084801	1
Caelo	Gelatine, white	17277207	1
Caelo	Gelatine, white	19090702	1
Caelo	Gelatine, white	11019308	1
Caelo	Gelatine, white	11334020	1
Caelo	Gelatine, white	12354507	3
Caelo	Gelatine, white	14130912	1
EuRho / 20	Gelatine, white	1106021-01	1
Euro OTC	Gelatine, white	1106021-01	2
Caelo	Gelatine, white	11334025	4

- 111 219 spectra from 742 *Apo-Ident* customers from a total of 31 873 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gelatine, white* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gelatine, white* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	125	0	110 564
Type B	0	80	0	119 062
Type C	0	27	1	111 219

The substance/substance group *Gelatine, white* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.2000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	96.4286 % (> 85.7143 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gelatine, white* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium citrate tetrahydrate	12.80	—
Cyanocobalamin	36.18	—
Heparin sodium	38.27	—
Bacitracin	39.59	—
Minoxidil	42.81	—
Levothyroxin sodium	46.49	—
Polymyxin B sulfate	46.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Gelatine, white* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22499	22499	0.00	12.93
22582	22582	0.00	12.80
20898	22582	6.52	17.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Gentamicin sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20640-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gentamicin sulfate; Gentamicin sulphate; Gentamicini sulfas

Special notes

When selecting the *Gentamicin sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Gentamicin sulfate	12	5	238

Second-stage model

For differentiation of the substance/substance group *Gentamicin sulfate* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Gentamicin sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Gentamicin sulfate	13205003	21580	60	20130723
Caelo	Gentamicin sulfate	14353504	22604	40	20150119
Euro OTC	Gentamicin sulfate	1305047-01	21081	30	20130919
Euro OTC	Gentamicin sulfate	1305047-03	21582	60	1411076
Euro OTC	Gentamicin sulfate	1305047-03	21697	45	AR-15-FG-012403-01
Euro OTC	Gentamicin sulfate	1506016	21837	60	0000010321
Euro OTC	Gentamicin sulfate	1610036	22857	40	20161124*
Euro OTC	Gentamicin sulfate	1610036-01	23782	40	1804343
Euro OTC	Gentamicin sulfate	1711025	23882	40	20171206*
Euro OTC	Gentamicin sulfate	1711025	23882SI	40	20171206*
Euro OTC	Gentamicin sulfate	1907036	24866	40	20190823*
Fagron	Gentamicin sulfate	12B21-N02	20661	40	1411075
Fagron	Gentamicin sulfate	14E08-B03-294848	21684	60	20140616
Fagron	Gentamicin sulfate	16B29-B01-328731	23210	40	20160411

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 635 spectra of 14 reference samples from the substance/substance group *Gentamicin sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 110 054 spectra from a total of 1954 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 540 spectra of 11 reference samples from the substance/substance group *Gentamicin sulfate*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Gentamicin sulfate	170996	23335	40
Caelo	Gentamicin sulfate	183001	24357	40
Euro OTC	Gentamicin sulfate	1604054	22568	40
Euro OTC	Gentamicin sulfate	1808013	24300	40
Fagron	Gentamicin sulfate	13I19-B05-286565	21578	60
Caelo	Gentamicin sulfate	13205003	21580SI [†]	60
Caelo	Gentamicin sulfate	183001	24357SI	40
Euro OTC	Gentamicin sulfate	1506016	21837SI [†]	60
Euro OTC	Gentamicin sulfate	1808013	24300SI	40
Fagron	Gentamicin sulfate	13I19-B05-286565	21578SI	60
Fagron	Gentamicin sulfate	14E08-B03-294848	21684SI [†]	60

- 118602 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1101 spectra from 456 *Apo-Ident* customers from 256 batches from the substance/substance group *Gentamicin sulfate*.
- Among them are spectra of independent samples from 237 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Gentamicin sulfate	15258818	26
AHD	Gentamicin sulfate	13205005	2
AHD /Pharmachem Pöckneck	Gentamicin sulfate	1506016-02	1
AHD 29.10.14 EK6,12	Gentamicin sulfate	13205004	1
Fagron	Gentamicin sulfate	14081307	2
AHD Lamotte GmbH	Gentamicin sulfate	1604054-02	1
Fagron	Gentamicin sulfate	14E08-B03-294841	1
ALH	Gentamicin sulfate	15258813	1
ALH	Gentamicin sulfate	15258816	1
Alliance Healthcare	Gentamicin sulfate	12G04-N16	1
Fagron	Gentamicin sulfate	13189607	1

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Anzag	Gentamicin sulfate	12146602	1
Anzag	Gentamicin sulfate	1305047-03	1
Anzag	Gentamicin sulfate	1407024-01	1
Euro OTC	Gentamicin sulfate	FG11112482	1
Apo Ident/ Noweda	Gentamicin sulfate	1711025	1
Audor Pharma	Gentamicin sulfate	1604054-01	1
Bombastus	Gentamicin sulfate	1205021-01	1
Bombastus	Gentamicin sulfate	700175	1
Bombastus	Gentamicin sulfate	17358616	1
Bombastus	Gentamicin sulfate	13024-N05	1
Caelo	Gentamicin sulfate	20161102-4	1
Caelo	Gentamicin sulfate	11113303	2
Caelo	Gentamicin sulfate	11113304	1
Caelo	Gentamicin sulfate	11113308	4
Caelo	Gentamicin sulfate	13091207	1
Caelo	Gentamicin sulfate	12163204	4
Caelo	Gentamicin sulfate	3110806	1
Caelo	Gentamicin sulfate	12163206	1
Caelo	Gentamicin sulfate	1710I-01582	1
Caelo	Gentamicin sulfate	12163207	3
Caelo	Gentamicin sulfate	1106016-03	1
Caelo	Gentamicin sulfate	12146602	8
Caelo	Gentamicin sulfate	12163209	1
Caelo	Gentamicin sulfate	1205021-01	1
Caelo	Gentamicin sulfate	12146604	6
Caelo	Gentamicin sulfate	1205021-02	2
Caelo	Gentamicin sulfate	12146611	11
Caelo	Gentamicin sulfate	12146612	2
Caelo	Gentamicin sulfate	6082013C	1
Caelo	Gentamicin sulfate	13189602	5
Caelo	Gentamicin sulfate	13189606	6
Caelo	Gentamicin sulfate	100017814	1
Caelo	Gentamicin sulfate	312012	1
Caelo	Gentamicin sulfate	31032014E	1
Caelo	Gentamicin sulfate	13189612	13
Caelo	Gentamicin sulfate	13189613	1
Caelo	Gentamicin sulfate	13205004	2
Caelo	Gentamicin sulfate	7011505	1
Caelo	Gentamicin sulfate	23012015E	1
Caelo	Gentamicin sulfate	14353503	13
Caelo	Gentamicin sulfate	130205005	1
Caelo	Gentamicin sulfate	13205007	2
Caelo	Gentamicin sulfate	1435303	1
Caelo	Gentamicin sulfate	17081502	1
Caelo	Gentamicin sulfate	8702	1
Caelo	Gentamicin sulfate	143533504	1
Caelo	Gentamicin sulfate	143535	1
Caelo	Gentamicin sulfate	14353505	3
Caelo	Gentamicin sulfate	2794	1
Caelo	Gentamicin sulfate	4563125	1
Caelo	Gentamicin sulfate	3714I-01582	1
Caelo	Gentamicin sulfate	FG1503073	1
Caelo	Gentamicin sulfate	15258810	14
Caelo	Gentamicin sulfate	150320G	1
Caelo	Gentamicin sulfate	1604054-02	1
Caelo	Gentamicin sulfate	16119302	1
Caelo	Gentamicin sulfate	15226517	1
Caelo	Gentamicin sulfate	15258819	6
Caelo	Gentamicin sulfate	16b29-b01-328731	1
Caelo	Gentamicin sulfate	17099601	2

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Gentamicin sulfate	17099606	13
Caelo	Gentamicin sulfate	12011801	1
Caelo	Gentamicin sulfate	18041804	1
Caelo	Gentamicin sulfate	1711025	1
Caelo	Gentamicin sulfate	17358604	3
Caelo	Gentamicin sulfate	17358609	28
Caelo	Gentamicin sulfate	1711025-02	3
Caelo	Gentamicin sulfate	17358618	2
Caelo	Gentamicin sulfate	17332419	1
Caelo	Gentamicin sulfate	18300103	1
Caelo	Gentamicin sulfate	17358619	1
Caelo	Gentamicin sulfate	18300108	3
Caelo	Gentamicin sulfate	18300109	4
Caelo	Gentamicin sulfate	15258816	15
Caelo	Gentamicin sulfate	15128818	1
Caelo	Gentamicin sulfate	14081307	1
Caelo	Gentamicin sulfate	17358603	23
Caelo	Gentamicin sulfate	17099606-20180404Ma1	1
Caelo	Gentamicin sulfate	15226513	1
Caelo	Gentamicin sulfate	15258805	1
Caelo	Gentamicin sulfate	1506016-02	2
Caelo	Gentamicin sulfate	14353502	2
Caelo	Gentamicin sulfate	1808013-01	2
Caelo	Gentamicin sulfate	13189607	11
Caelo	Gentamicin sulfate	1305047-03(2ma1)	1
Caelo	Gentamicin sulfate	17358607	1
Caelo	Gentamicin sulfate	1506016-01	2
Caelo	Gentamicin sulfate	1528818	1
Caelo	Gentamicin sulfate	18Go6-351916	1
Caelo	Gentamicin sulfate	15226508	2
Caelo	Gentamicin sulfate	3265	1
Caelo	Gentamicin sulfate	161003602	1
Caelo	Gentamicin sulfate	18300113	7
Caelo	Gentamicin sulfate	13D24-N05	1
Caelo	Gentamicin sulfate	17358616	18
Caelo	Gentamicin sulfate	12G04-N16	2
Caelo	Gentamicin sulfate	15B03-B07-309482	1
Caelo	Gentamicin sulfate	14K28-B06-303636	1
Caelo	Gentamicin sulfate	15258802	14
Caelo	Gentamicin sulfate	15258808	8
Caelo	Gentamicin sulfate	20170829/1	1
Caelo	Gentamicin sulfate	13189608	2
Caelo	Gentamicin sulfate	14E08-B03-294841	1
Caelo	Gentamicin sulfate	14K28-B06-303646	3
Caelo	Gentamicin sulfate	1528802	1
Caelo	Gentamicin sulfate	15226518	7
Caelo	Gentamicin sulfate	115258818	1
Caelo	Gentamicin sulfate	1709601	1
Caelo	Gentamicin sulfate	17099608	16
Caelo	Gentamicin sulfate	180801301	2
Caelo	Gentamicin sulfate	18300104	11
Fagron	Gentamicin sulfate	17099606	1
Caelo	Gentamicin sulfate	13189611	9
Caelo	Gentamicin sulfate	13205005	14
Caelo	Gentamicin sulfate	15258803	13
Caelo	Gentamicin sulfate	1604054-01	3
Caelo	Gentamicin sulfate	15258813	13
Caelo	Gentamicin sulfate	17099603	23
Caelo	Gentamicin sulfate	1711025-01	1
Caelo	Gentamicin sulfate	17358610	5

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Gentamicin sulfate	18300112	1
Caelo	Gentamicin sulfate	73402189	1
Caelo	Gentamicin sulfate	13205006	6
Caelo	Gentamicin sulfate	15226502	14
Caelo	Gentamicin sulfate	1610036-01	6
Caelo	Gentamicin sulfate	15258815	3
Caelo	Gentamicin sulfate	15258825	2
Caelo	Gentamicin sulfate	1522650217099604	1
Caelo	Gentamicin sulfate	18G06-B09-354797	1
Caelo	Gentamicin sulfate	12146605	4
Caelo	Gentamicin sulfate	15226501	16
Caelo	Gentamicin sulfate	15226514	5
Caelo	Gentamicin sulfate	FG1603072	1
Caelo	Gentamicin sulfate	17099604	14
Caelo	Gentamicin sulfate	13189603	3
Caesar & Loretz GmbH	Gentamicin sulfate	14353503	1
Caesar & Loretz GmbH	Gentamicin sulfate	17358610	1
Caesar & Loretz GmbH	Gentamicin sulfate	17358607	1
Caesar & Loretz GmbH	Gentamicin sulfate	17358618	1
Caesar & Loretz GmbH	Gentamicin sulfate	18300104	2
Caesar & Loretz GmbH	Gentamicin sulfate	18300103	1
Caesar & Loretz GmbH	Gentamicin sulfate	18300108	2
Caesar & Loretz GmbH	Gentamicin sulfate	17099604	1
Caesar & Loretz GmbH / ...	Gentamicin sulfate	18300113	1
Caesar & Loretz GmbH, A...	Gentamicin sulfate	17358603	1
Caesar & Loretz GmbH/No...	Gentamicin sulfate	18300104	1
Caesar&Loretz GmbH	Gentamicin sulfate	15226501	1
Caesar&Loretz GmbH,25.0...	Gentamicin sulfate	15258802	1
Celo/Jenne	Gentamicin sulfate	17099603	1
Delta Apotheke	Gentamicin sulfate	17358604	2
eurho	Gentamicin sulfate	1711025-01	1
EuRho	Gentamicin sulfate	1106016-03	1
EuRho	Gentamicin sulfate	FG1112482	1
EuRho	Gentamicin sulfate	1305047-01	1
EuRho	Gentamicin sulfate	1808013-01	4
EuRho / Phönix	Gentamicin sulfate	1610036-02	1
Eurho/Noweda	Gentamicin sulfate	1604054-02	1
Eurimpharm1	Gentamicin sulfate	1604054-01	1
euro AHD	Gentamicin sulfate	1711025-015586	1
Euro OTC	Gentamicin sulfate	1407024-01	5
Euro OTC	Gentamicin sulfate	160405401	1
Euro OTC	Gentamicin sulfate	1407024-04	5
Euro OTC	Gentamicin sulfate	1106016-03	5
Euro OTC	Gentamicin sulfate	2911034-02	1
Euro OTC	Gentamicin sulfate	130504701	1
Euro OTC	Gentamicin sulfate	130504703	2
Euro OTC	Gentamicin sulfate	FG1501009	1
Euro OTC	Gentamicin sulfate	161003601	3
Euro OTC	Gentamicin sulfate	1610036-015339	1
Euro OTC	Gentamicin sulfate	190703601	2
Euro OTC	Gentamicin sulfate	1907036-01	2
Euro OTC	Gentamicin sulfate	171102502	1
Euro OTC	Gentamicin sulfate	1506016-01	14
Euro OTC	Gentamicin sulfate	17358609	2
Euro OTC	Gentamicin sulfate	1711025-02	5
Euro OTC	Gentamicin sulfate	150601602	2
Euro OTC	Gentamicin sulfate	1305047	1
Euro OTC	Gentamicin sulfate	1407024-03	2
Euro OTC	Gentamicin sulfate	1610036-02	11
Euro OTC	Gentamicin sulfate	1205021-02	17

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Gentamicin sulfate	80616-2	1
Euro OTC	Gentamicin sulfate	1604054-03	2
Euro OTC	Gentamicin sulfate	1106016-01	3
Euro OTC	Gentamicin sulfate	150601601	1
Euro OTC	Gentamicin sulfate	1407024-02	1
Euro OTC	Gentamicin sulfate	1808013-01	6
Euro OTC	Gentamicin sulfate	180208G/1711025-01	1
Euro OTC	Gentamicin sulfate	4988304	1
Euro OTC	Gentamicin sulfate	1808013-02	6
Euro OTC	Gentamicin sulfate	1205021-01	12
Euro OTC	Gentamicin sulfate	140702403	1
Euro OTC	Gentamicin sulfate	15258816	1
Euroo/Phoenix	Gentamicin sulfate	1305047-03	1
Euro OTC	Gentamicin sulfate	1407024	1
Euro OTC	Gentamicin sulfate	140702404	3
Euro OTC	Gentamicin sulfate	1604054-02	7
Euro OTC	Gentamicin sulfate	1711025-01	23
Euro OTC	Gentamicin sulfate	1506016-02	26
Euro OTC	Gentamicin sulfate	1604054-3	1
Fagron	Gentamicin sulfate	10A29-N06	1
Fagron	Gentamicin sulfate	11/09-N10	1
Fagron	Gentamicin sulfate	12G04-N16	2
Fagron	Gentamicin sulfate	12D6-N05	1
Fagron	Gentamicin sulfate	13D24-N05	8
Fagron	Gentamicin sulfate	1106016-01	1
Fagron	Gentamicin sulfate	1205021-02	1
Fagron	Gentamicin sulfate	13/19-B05-286568	1
Fagron	Gentamicin sulfate	14A30-B04-290861	2
Fagron	Gentamicin sulfate	14A30-B04	3
Fagron	Gentamicin sulfate	19-B05-286568	1
Fagron	Gentamicin sulfate	13F13-N01	1
Fagron	Gentamicin sulfate	14a30-b04-290858	1
Fagron	Gentamicin sulfate	14E08-B03	2
Fagron	Gentamicin sulfate	14E08-B03-300619	1
Fagron	Gentamicin sulfate	14K28-B06-301951	1
Fagron	Gentamicin sulfate	14k28-b06-303640	2
Fagron	Gentamicin sulfate	15b03-b07-309482	1
Fagron	Gentamicin sulfate	15B03-B07	1
Fagron	Gentamicin sulfate	15G29-B09-320305	3
Fagron	Gentamicin sulfate	15803-B07-309482	1
Fagron	Gentamicin sulfate	15E04-B05-319740	1
Fagron	Gentamicin sulfate	15G29-B09-326632	4
Fagron	Gentamicin sulfate	15G29-B09-322936	2
Fagron	Gentamicin sulfate	10C22N02	1
Fagron	Gentamicin sulfate	15G29B09322936	1
Fagron	Gentamicin sulfate	15G29-B09-326635	1
Fagron	Gentamicin sulfate	15G29-B09-322928	1
Fagron	Gentamicin sulfate	16829-B01-328731	1
Fagron	Gentamicin sulfate	17G27-B05	1
Fagron	Gentamicin sulfate	17G27-B05-340121	1
Fagron	Gentamicin sulfate	FG1709255	1
Fagron	Gentamicin sulfate	14K28-B06-303646	5
Fagron	Gentamicin sulfate	19A22-B05-191434	2
Fagron	Gentamicin sulfate	14k28-B06-303640	1
Fagron	Gentamicin sulfate	14e08b03300619	1
Fagron	Gentamicin sulfate	19G17-B05-193462	1
Fagron	Gentamicin sulfate	18C12-B02-350204	2
Fagron	Gentamicin sulfate	FG1305122	1
Fagron	Gentamicin sulfate	14E08-B03-294835	2
Fagron	Gentamicin sulfate	15258802	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Gentamicin sulfate	16B29-B01-328915	1
Fagron	Gentamicin sulfate	17099608	1
Fagron	Gentamicin sulfate	18G06-B09	1
Fagron	Gentamicin sulfate	13/19-B05	1
Fagron	Gentamicin sulfate	5214A-01582	1
Fagron	Gentamicin sulfate	1221-n02	1
Fagron	Gentamicin sulfate	13I19-B05-286568	1
Fagron	Gentamicin sulfate	11604054-01	1
Fagron	Gentamicin sulfate	11K21-N17	2
Fagron	Gentamicin sulfate	14K28-B06	3
Fagron	Gentamicin sulfate	14K28-B06-303640	3
Fagron	Gentamicin sulfate	18C12-B02-349025	6
Fagron	Gentamicin sulfate	18C12-B02	2
Fagron	Gentamicin sulfate	14A30-B04-290858	1
Fagron	Gentamicin sulfate	15G29-B09-322945	1
Fagron	Gentamicin sulfate	15121722	2
Fagron	Gentamicin sulfate	18C12-B02-350	1
Fagron	Gentamicin sulfate	18C12B02350204	1
Fagron	Gentamicin sulfate	18G06-B09-351916	4
Fagron	Gentamicin sulfate	12D26-N05	9
Fagron	Gentamicin sulfate	1319-B05-286565	1
Fagron	Gentamicin sulfate	FG1212646	1
Fagron	Gentamicin sulfate	15E04-B05-316255	2
Fagron	Gentamicin sulfate	15G29B0932632	1
Fagron	Gentamicin sulfate	16B29-B01	1
Fagron	Gentamicin sulfate	1711025-01	1
Fagron	Gentamicin sulfate	18G06-B09-354797	1
Fagron	Gentamicin sulfate	180810051	1
Fagron	Gentamicin sulfate	11k21-n17	1
Fagron	Gentamicin sulfate	12117-no2	1
Fargon	Gentamicin sulfate	13D24-N05	1
Fargon/AHD	Gentamicin sulfate	12G04-N16	1
Fujian	Gentamicin sulfate	FG1706157	1
Fujian Fukang Pharmacea...	Gentamicin sulfate	14A30-B04-290861	1
Fujian Fukang Pharmacea...	Gentamicin sulfate	14E08-B03-300619	1
Fujian Fukang Pharmaceu...	Gentamicin sulfate	12G04-N16	2
Fujian Fukang Pharmaceu...	Gentamicin sulfate	14E08-B03-294848	1
Gehe	Gentamicin sulfate	12146604	1
Gehe	Gentamicin sulfate	FG1307194	1
Gehe	Gentamicin sulfate	15226517	1
Gehe	Gentamicin sulfate	1711025-01	1
Gehe	Gentamicin sulfate	17358609	1
Gehe	Gentamicin sulfate	18300109	2
Gehe	Gentamicin sulfate	18300108	1
GEHE	Gentamicin sulfate	15258815	1
GEHE	Gentamicin sulfate	15258808	1
GEHE	Gentamicin sulfate	17358603	2
GEHE	Gentamicin sulfate	17358609	1
GEHE	Gentamicin sulfate	18300109	1
Gehe am 24.2.14	Gentamicin sulfate	1305047-01	1
Caelo	Gentamicin sulfate	1260417	1
Gehe/Euro	Gentamicin sulfate	1610036-02	1
Fagron	Gentamicin sulfate	15258816	2
Euro OTC	Gentamicin sulfate	1106016-02	3
Ichthyol/ALH	Gentamicin sulfate	15258810	1
Euro OTC	Gentamicin sulfate	1604054-01	18
Euro OTC	Gentamicin sulfate	1907035-01	1
Kehr	Gentamicin sulfate	110036-02	1
Klosterring	Gentamicin sulfate	15G29-B09	1
Nachprüfung	Gentamicin sulfate	123456	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Noweda	Gentamicin sulfate	12146602	1
Noweda	Gentamicin sulfate	13189607	1
Noweda	Gentamicin sulfate	13189611	1
Noweda	Gentamicin sulfate	13189612	1
Noweda	Gentamicin sulfate	1305005	1
Noweda	Gentamicin sulfate	140702404	1
Noweda	Gentamicin sulfate	14353504	1
Noweda	Gentamicin sulfate	15258818	1
Noweda	Gentamicin sulfate	17358616	1
Noweda	Gentamicin sulfate	17358623	1
Noweda	Gentamicin sulfate	18300108	2
Caelo	Gentamicin sulfate	15258809	1
Fagron	Gentamicin sulfate	14K28B06303646	2
Fagron	Gentamicin sulfate	15B03-B07-309482	1
Phoenix	Gentamicin sulfate	12D26-N05	1
Phoenix	Gentamicin sulfate	1305047-03	1
Phoenix	Gentamicin sulfate	15226502	1
Phoenix	Gentamicin sulfate	15226501	1
Phoenix	Gentamicin sulfate	15258816	1
Phoenix	Gentamicin sulfate	1604054-02	1
Phoenix	Gentamicin sulfate	16b29-b01-328731	1
Phoenix	Gentamicin sulfate	17099603	1
Phoenix	Gentamicin sulfate	17G27-B05-340121	1
Phoenix	Gentamicin sulfate	17358603	1
Phoenix	Gentamicin sulfate	1711025-02	2
Phoenix	Gentamicin sulfate	3404	1
Phoenix	Gentamicin sulfate	18300113	1
PHOENIX 10.03.2014	Gentamicin sulfate	1305047	1
Caelo	Gentamicin sulfate	13I19-B05-286565	1
phönix	Gentamicin sulfate	1214605	1
Phönix	Gentamicin sulfate	11113309	1
Phönix	Gentamicin sulfate	12146602	1
Phönix	Gentamicin sulfate	13189611	1
Phönix	Gentamicin sulfate	14353502	1
Phönix	Gentamicin sulfate	17099603	1
Phönix	Gentamicin sulfate	3141	1
PHÖNIX	Gentamicin sulfate	15226514	1
Caelo	Gentamicin sulfate	16B29-B01-328731	1
Phönix Gotha	Gentamicin sulfate	13189611	1
Sanacorp	Gentamicin sulfate	13189607	1
Sanacorp	Gentamicin sulfate	13189608	1
Sanacorp	Gentamicin sulfate	1305047-03	1
Sanacorp	Gentamicin sulfate	161003601	1
Sanacorp	Gentamicin sulfate	1610036-01	2
Sanacorp	Gentamicin sulfate	FG1711309	1
Sanacorp	Gentamicin sulfate	17358604	1
Sanacorp	Gentamicin sulfate	18C12-B02-349026	1
Sanacorp	Gentamicin sulfate	17358618	1
Caelo	Gentamicin sulfate	13189614	2
Caelo	Gentamicin sulfate	1305047-03	3
Sanacorp 06.01.15 EK 6,20	Gentamicin sulfate	1305047-03	1
Sanacorp WE: 28.09.17 ...	Gentamicin sulfate	15258825	1
Euro OTC	Gentamicin sulfate	4318A-01582	1
Fagron	Gentamicin sulfate	13I19-B05	1
vdl	Gentamicin sulfate	12146602	1
Caelo	Gentamicin sulfate	1106016-01	1
Yantai Justaware Ph.-CN...	Gentamicin sulfate	14K28-B06_303646	1
Yantai Justaware Ph.-CN...	Gentamicin sulfate	14081307	1
Yantai Justaware Pharma...	Gentamicin sulfate	14K28-B06	1
Euro OTC	Gentamicin sulfate	1610036-01	16

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Supplier	Substance	Batch	Spectra
Caelo	Gentamicin sulfate	13205003	10
Caelo	Gentamicin sulfate	14353504	11
Caelo	Gentamicin sulfate		3
	Gentamicin sulfate	1610038-01	1
Euro OTC	Gentamicin sulfate	1305047-03	11
Euro OTC	Gentamicin sulfate	1305047-01	9
Fagron	Gentamicin sulfate	16B29-B01-328731	4
Fagron	Gentamicin sulfate	12B21-N02	2
Fagron	Gentamicin sulfate	14E08-B03-294848	4
Euro OTC	Gentamicin sulfate		1

- 110 146 spectra from 742 *Apo-Ident* customers from a total of 31 641 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gentamicin sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gentamicin sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	635	0	110 054
Type B	0	475	65	118 602
Type C	0	1042	59	110 146

The substance/substance group *Gentamicin sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0551 %)
Type B	100.0000 % (> 99.9893 %)	87.9630 % (> 87.4074 %)
Type C	100.0000 % (> 99.8899 %)	94.6412 % (> 94.3688 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gentamicin sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium hydrogen citrate	27.70	—
Arginine hydrochloride	35.40	—
Levothyroxin sodium	38.29	—
Magnesium citrate	39.85	—
Calcium colamine phosphate	45.94	—
Riboflavin phosphate sodium	53.18	—
⋮	⋮	⋮
Sodium citrate	55.07	122.42
Beclometasone dipropionate	>50	239.82
Clobetasol propionate	>50	243.34
Betamethasone dipropionate, micronized	>50	273.67
Oxybutynin hydrochloride	>50	306.35
Sodium benzoate	>50	946.40

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Gentamicin sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24866	24866	0.00	39.64
21697	21697	0.00	41.74
22857	22857	0.00	38.40
21684	21582	2.93	36.52
21081	21837	3.03	37.53
22604	21837	1.96	37.75
21837	21837	0.00	37.12
21582	21582	0.00	37.58
21580	21837	3.99	37.36
23782	23782	0.00	39.59
23210	24866	2.27	38.00
20661	20661	0.00	37.60
23882	23882	0.00	39.71

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glucose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20982-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glucose; Glucosum

Special notes

When selecting the *Glucose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glucose	5	2	172

Second-stage model

For differentiation of the substance/substance group *Glucose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glucose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Glucose	12294514	20982	40	1402475
Caelo	Glucose	14033901	21363	40	20140214
Caelo	Glucose	14142310	21703	45	20140523
Caelo	Glucose	16050501	22586	40	20160317
Caelo	Glucose	190380	24511	40	20190411*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 205 spectra of 5 reference samples from the substance/substance group *Glucose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 484 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Glucose*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Glucose	16157401	23583	40
Caelo	Glucose	180129	23820	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 619 spectra from 130 *Apo-Ident* customers from 177 batches from the substance/substance group *Glucose*.
- Among them are spectra of independent samples from 171 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
21.03.2017	Glucose	6910499	1
Caelo	Glucose	16328801	12
AHD	Glucose	14033908	1
Caelo	Glucose	15148802	6
Caelo	Glucose	15095001	8
Caelo	Glucose	15329001	6
Caelo	Glucose	15329006	9
Caelo	Glucose	16157403	24
Allianc. Healthc. /c	Glucose	16050510	1
Caelo	Glucose	14142303	3
Caelo	Glucose	14142308	1
Caelo	Glucose	14142314	3
Fagron	Glucose	13178716	1
Fagron	Glucose	14142303	1
Anzag	Glucose	13329505	1
Caelo	Glucose	16050507	2
Euro OTC	Glucose	18012905	3
Apotheke-SiO2-Mischung	Glucose	18/15	1
Audor Pharma	Glucose	16157402	3
Bombastus	Glucose	160505202	1
Caelo	Glucose	16328803	9
Caelo	Glucose	106213393	1
Caelo	Glucose	25061204	1
Caelo	Glucose	208223393	1
Caelo	Glucose	16101204	1
Caelo	Glucose	16101205	1
Caelo	Glucose	712213393	1
Caelo	Glucose	402313393	2
Caelo	Glucose	1001313393	1
Caelo	Glucose	2102201301	1
Caelo	Glucose	12294509	2
Caelo	Glucose	12294505	3
Caelo	Glucose	26041303	1
Caelo	Glucose	15051301	1
Caelo	Glucose	2013Q-03393	1
Caelo	Glucose	12294515	2

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Supplier	Substance	Batch	Spectra
Caelo	Glucose	2513M03393	1
Caelo	Glucose	13178711	2
Caelo	Glucose	13178707	2
Caelo	Glucose	13178715	4
Caelo	Glucose	13178718	1
Caelo	Glucose	1317815	1
Caelo	Glucose	13329504	2
Caelo	Glucose	13329507	1
Caelo	Glucose	14051401	1
Caelo	Glucose	5081401	1
Caelo	Glucose	13178701	2
Caelo	Glucose	14142301	1
Caelo	Glucose	23091401	1
Caelo	Glucose	14142304	1
Caelo	Glucose	3121402	1
Caelo	Glucose	13178712	1
Caelo	Glucose	14142313	2
Caelo	Glucose	14319302	1
Caelo	Glucose	14319304	6
Caelo	Glucose	6031505	1
Caelo	Glucose	13041501	1
Caelo	Glucose	14319309	3
Caelo	Glucose	1439304	1
Caelo	Glucose	4071505	1
Caelo	Glucose	15095005	2
Caelo	Glucose	15148809	1
Caelo	Glucose	10091503	1
Caelo	Glucose	15095003	2
Caelo	Glucose	1509500	3
Caelo	Glucose	15329005	4
Caelo	Glucose	15329008	1
Caelo	Glucose	16050504	1
Caelo	Glucose	15329002	2
Caelo	Glucose	16050502	9
Caelo	Glucose	16050503	16
Caelo	Glucose	15329010	2
Caelo	Glucose	16050510	2
Caelo	Glucose	160308G	1
Caelo	Glucose	16157406	18
Caelo	Glucose	8031703	1
Caelo	Glucose	17041701	1
Caelo	Glucose	16157411	7
Caelo	Glucose	2051701	1
Caelo	Glucose	1061703	1
Caelo	Glucose	6071717	1
Caelo	Glucose	7091705	1
Caelo	Glucose	18111702	1
Caelo	Glucose	28111714	1
Caelo	Glucose	16328812	12
Caelo	Glucose	15021801	1
Caelo	Glucose	16328811	2
Caelo	Glucose	12041801	1
Caelo	Glucose	14051802	1
Caelo	Glucose	18012907	20
Caelo	Glucose	120718A	1
Caelo	Glucose	15081831	1
Caelo	Glucose	8091810	1
Caelo	Glucose	17111803	1
Caelo	Glucose	2021902	1
Caelo	Glucose	18012922	1

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Supplier	Substance	Batch	Spectra
Caelo	Glucose	1801290246/18	1
Caelo	Glucose	13329503	3
Caelo	Glucose	15148803	1
Caelo	Glucose	15095004	3
Caelo	Glucose	11358823	1
Caelo	Glucose	3214M-03393	1
Caelo	Glucose	12141718	3
Caelo	Glucose	12141717	1
Caelo	Glucose	12294519	1
Caelo	Glucose	14033908	2
Caelo	Glucose	14319308	1
Caelo	Glucose	1650502	1
Caelo	Glucose	14033902	4
Caelo	Glucose	12294510	3
Caelo	Glucose	13178702	1
Caelo	Glucose	18012921	13
Caelo	Glucose	18012905	6
Caelo	Glucose	18012913	5
Caelo	Glucose	1614U3393	1
Caelo	Glucose	18012914	9
Caelo	Glucose	19038002	17
Caelo	Glucose	18012911	6
Caelo	Glucose	12141705	1
Caelo	Glucose	13329512	7
Caelo	Glucose	14033907	5
Caelo	Glucose	15148810	4
Caelo	Glucose	18012902	17
Caelo	Glucose	18012915	14
Caelo	Glucose	19038007	1
Caelo	Glucose	18012912	11
Caelo	Glucose	1415U-03393	1
Caelo	Glucose	1812913	1
Caelo	Glucose	12141714	2
Caelo	Glucose	12141715	1
Caelo	Glucose	13178716	1
Caelo	Glucose	13329501	3
Caelo	Glucose	1114A03393	1
Caelo	Glucose	1914I03393	1
Caelo	Glucose	15329004	4
Caelo	Glucose	12294517	1
Caelo	Glucose	15148813	1
Caelo	Glucose	551616157406	1
Caelo	Glucose	18012923	2
Caelo	Glucose	19038005	3
Caelo	Glucose	19038006	2
Caelo	Glucose	19028005	1
Caelo	Glucose	3513I-03393	1
Caelo	Glucose	4313Q3393	1
Caelo	Glucose	5013I3393	1
Caelo	Glucose	15148808	3
Caelo	Glucose	16328805	15
Caelo	Glucose	16328807	6
Caelo	Glucose	18012917	2
Caelo	Glucose	2x18012915	1
Caelo	Glucose	47131-03393	1
Caelo	Glucose	214U-03393	1
Caelo	Glucose	14319310	2
Caelo	Glucose	15148801	4
Caelo	Glucose	16050508	1
Caelo	Glucose	16157402	4

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Supplier	Substance	Batch	Spectra
Caelo	Glucose	19038001	4
Caelo	Glucose	12294509-3425311150	1
Caelo	Glucose	16328813	1
Caelo	Glucose	18012910	2
Caelo	Glucose	18012916	1
Caelo	Glucose	19038003	1
Caesar & Loretz GmbH	Glucose	16157403	1
Caesar & Loretz GmbH	Glucose	18012912	1
Caesar & Loretz GmbH	Glucose	18012921	5
Caesar & Loretz GmbH	Glucose	18012915	2
Caesar & Loretz GmbH	Glucose	18012926	1
Caesar & Loretz GmbH	Glucose	19038007	2
Caesar&Loretz	Glucose	15148808	1
Caesar&loretz,Anzag	Glucose	12294509	1
Euro OTC	Glucose	15148808	1
Euro OTC	Glucose	16050502	2
Euro OTC	Glucose	18012922	1
Fagron	Glucose	15329005	2
Gehe	Glucose	16157403	2
GEHE	Glucose	13178715	1
GEHE	Glucose	16157406	1
GEHE	Glucose	16328801	1
GEHE	Glucose	16328805	1
GEHE	Glucose	18012902	2
GEHE	Glucose	18012907	3
GEHE	Glucose	18012912	1
GEHE	Glucose	18012915	4
GEHE	Glucose	19038002	2
GEHE 17.07.2014	Glucose	14033907	1
Gehe 27.11.14	Glucose	14142309	1
Gehe Kassel	Glucose	14142313	1
Caelo	Glucose	13178704	3
Caelo	Glucose	14033906	5
Ichtyol-Ges HH/Sanacorp	Glucose	18012909	1
Jenne	Glucose	12141705	1
Klenk	Glucose	16050502	1
Caelo	Glucose	15148807	4
Phoenix	Glucose	14142310	1
Phoenix	Glucose	15329010	2
Phoenix	Glucose	15148801	1
Phoenix	Glucose	16050503	4
Phoenix	Glucose	16050501	1
PHOENIX 30.05.2014	Glucose	14033902	1
PHOENIX 30.05.2014	Glucose	13329514	1
Phönix	Glucose	13178701	1
PHÖNIX	Glucose	16328805	2
PHÖNIX	Glucose	16328812	3
PHÖNIX	Glucose	18012902	1
Caelo	Glucose	18012909	4
Phönix/Fagon	Glucose	16328807	1
Rondell Apotheke	Glucose	15329003	1
Sanacorp	Glucose	12294509	1
Caelo	Glucose	18012903	3
Caelo	Glucose	AKD14	1
Caelo	Glucose	18012920	4
Sonnen-Apotheke Wefensl...	Glucose	17/16	1
Sonnen-Apotheke Wefensl...	Glucose	34/16	1
Sonnen-Apotheke Wefensl...	Glucose	21/17Glucose-Si02-M	1
Caelo	Glucose	12141706	3

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Supplier	Substance	Batch	Spectra
Apotheke/Defektur Misch. ...	Glucose		1
Caelo	Glucose	12294514	2
Caelo	Glucose	14142310	4
Caelo	Glucose	16050501	12
Caelo	Glucose	14033901	2
Nachprüfung	Glucose		1

- 110 628 spectra from 742 *Apo-Ident* customers from a total of 31 716 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glucose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glucose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	205	0	110 484
Type B	0	80	0	119 062
Type C	0	602	17	110 628

The substance/substance group *Glucose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0732 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	97.2536 % (> 96.7690 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glucose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Aciclovir	38.84	—
Neomycin sulfate	52.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glucose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20982	20982	0.00	36.80
21363	24511	9.52	39.44
21703	20982	4.94	38.43
24511	24511	0.00	41.24
22586	20982	3.14	38.23

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glucose monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20031-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glucose monohydrate; Glucosum monohydricum

Special notes

When selecting the *Glucose monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glucose monohydrate	9	11	324

Second-stage model

For differentiation of the substance/substance group *Glucose monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glucose monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Glucose monohydr...	171368	23304	40	20170601*
Caelo	Glucose monohydr...	173050	23802	40	20171110*
Euro OTC	Glucose monohydr...	1509006	21905	60	20150914*
Euro OTC	Glucose monohydr...	1601016	22308	60	20160129*
Euro OTC	Glucose monohydr...	1604006	22538	40	20160511*
Euro OTC	Glucose monohydr...	1701002	23006	40	20170213*
Euro OTC	Glucose monohydr...	1807005	24162	40	20180718*
Fagron	Glucose monohydr...	11L19-N13	20799	40	20120105
Fagron	Glucose monohydr...	14B04-B01	21274	40	20140304

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 9 reference samples from the substance/substance group *Glucose monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 289 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 440 spectra of 11 reference samples from the substance/substance group *Glucose monohydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Glucose monohydrate	16184807	23025	40
Caelo	Glucose monohydrate	190733	24506	40
Caelo	Glucose monohydrate	182174	24906	40
Euro OTC	Glucose monohydrate	1210034-02	21285	40
Euro OTC	Glucose monohydrate	1607024	22692	40
Euro OTC	Glucose monohydrate	1707004	23545	40
Euro OTC	Glucose monohydrate	1801009	23897	40
Euro OTC	Glucose monohydrate	1811020	24418	40
Euro OTC	Glucose monohydrate	1904029	24640	40
Euro OTC	Glucose monohydrate	1908012	24860	40
Euro OTC	Glucose monohydrate	2001006	25083	40

- 118 702 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1618 spectra from 370 *Apo-Ident* customers from 332 batches from the substance/substance group *Glucose monohydrate*.
- Among them are spectra of independent samples from 324 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Glucose monohydrate	KNC1282J14	1
ACM	Glucose monohydrate	KNC1164J15	1
AHD	Glucose monohydrate	14102407	1
Bombastus	Glucose monohydrate	14334802	2
Caelo	Glucose monohydrate	15413303	1
Caelo	Glucose monohydrate	16184816	2
Caelo	Glucose monohydrate	17136801	17
Alliance	Glucose monohydrate	16049101	1
allianz	Glucose monohydrate	1543409	1
Anzag	Glucose monohydrate	14334810	1
Anzag	Glucose monohydrate	16184808	1
Anzag	Glucose monohydrate	17005804	1
Anzag	Glucose monohydrate	17136805	1
apo-ident	Glucose monohydrate	1604006-02	1
Apo-Ident/Phoenix	Glucose monohydrate	1701002-01	1
Apo-Ident/Phoenix	Glucose monohydrate	1707004-01	3
Apotheke im Forum	Glucose monohydrate	17010002-01	1
Beiersdorf/Phönix	Glucose monohydrate	L6209	1
Bombastus	Glucose monohydrate	1807005-01	1
Bombastus	Glucose monohydrate	15413410	1
Bombastus	Glucose monohydrate	16184810	2
Caello/Phönix	Glucose monohydrate	15095601	3

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Glucose monohydrate	11082020	1
Caelo	Glucose monohydrate	13157022	1
Caelo	Glucose monohydrate	15180002	15
Caelo	Glucose monohydrate	2316E-02209	1
Caelo	Glucose monohydrate	17005811	2
Caelo	Glucose monohydrate	11082014	1
Caelo	Glucose monohydrate	10159501	1
Caelo	Glucose monohydrate	1134506	1
Caelo	Glucose monohydrate	11L19-N13	3
Caelo	Glucose monohydrate	12G30-N001	1
Caelo	Glucose monohydrate	12284202	6
Caelo	Glucose monohydrate	12284204	2
Caelo	Glucose monohydrate	11314519	1
Caelo	Glucose monohydrate	13157002	2
Caelo	Glucose monohydrate	13157008	1
Caelo	Glucose monohydrate	E144C	1
Caelo	Glucose monohydrate	13157004	1
Caelo	Glucose monohydrate	13157019	10
Caelo	Glucose monohydrate	12284231	1
Caelo	Glucose monohydrate	5051401	1
Caelo	Glucose monohydrate	18071402	1
Caelo	Glucose monohydrate	14102407	2
Caelo	Glucose monohydrate	2101402	1
Caelo	Glucose monohydrate	14102416	5
Caelo	Glucose monohydrate	14102420	5
Caelo	Glucose monohydrate	14102427	1
Caelo	Glucose monohydrate	14102415	1
Caelo	Glucose monohydrate	11021509	1
Caelo	Glucose monohydrate	14B28-B02-291354	1
Caelo	Glucose monohydrate	200415PJK01	1
Caelo	Glucose monohydrate	14334811	2
Caelo	Glucose monohydrate	15095601	8
Caelo	Glucose monohydrate	28051507	1
Caelo	Glucose monohydrate	15095611	3
Caelo	Glucose monohydrate	15095612	13
Caelo	Glucose monohydrate	15180005	3
Caelo	Glucose monohydrate	15180001	12
Caelo	Glucose monohydrate	15180003	3
Caelo	Glucose monohydrate	8697	1
Caelo	Glucose monohydrate	15180009	1
Caelo	Glucose monohydrate	15180015	7
Caelo	Glucose monohydrate	2315Q-02209NP	1
Caelo	Glucose monohydrate	2743	1
Caelo	Glucose monohydrate	15180016	2
Caelo	Glucose monohydrate	2745	1
Caelo	Glucose monohydrate	15413410	3
Caelo	Glucose monohydrate	613011-3p	1
Caelo	Glucose monohydrate	15413409	23
Caelo	Glucose monohydrate	160101	1
Caelo	Glucose monohydrate	15413413	1
Caelo	Glucose monohydrate	15413301	1
Caelo	Glucose monohydrate	2795	1
Caelo	Glucose monohydrate	16049103	4
Caelo	Glucose monohydrate	1604006-01	1
Caelo	Glucose monohydrate	1604104	1
Caelo	Glucose monohydrate	150302G	1
Caelo	Glucose monohydrate	16049107	6
Caelo	Glucose monohydrate	16184810	23
Caelo	Glucose monohydrate	16184807	10
Caelo	Glucose monohydrate	17005803	22

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Glucose monohydrate	1607024-01	1
Caelo	Glucose monohydrate	170058025312	1
Caelo	Glucose monohydrate	219317005803	1
Caelo	Glucose monohydrate	17005805	2
Caelo	Glucose monohydrate	1701002-01	2
Caelo	Glucose monohydrate	170058025458	1
Caelo	Glucose monohydrate	170058025517	1
Caelo	Glucose monohydrate	17305004	8
Caelo	Glucose monohydrate	23051801	1
Caelo	Glucose monohydrate	26061802	1
Caelo	Glucose monohydrate	18101901	23
Caelo	Glucose monohydrate	181401903	1
Caelo	Glucose monohydrate	24081801	1
Caelo	Glucose monohydrate	27081801	1
Caelo	Glucose monohydrate	18101907	18
Caelo	Glucose monohydrate	1801009-01	2
Caelo	Glucose monohydrate	1810901	1
Caelo	Glucose monohydrate	18214703	19
Caelo	Glucose monohydrate	181197	1
Caelo	Glucose monohydrate	19073303	8
Caelo	Glucose monohydrate	14334807	4
Caelo	Glucose monohydrate	15095605	3
Caelo	Glucose monohydrate	17005812	3
Caelo	Glucose monohydrate	15180013	2
Caelo	Glucose monohydrate	16184802	2
Caelo	Glucose monohydrate	1305030-02	1
Caelo	Glucose monohydrate	14102401	4
Caelo	Glucose monohydrate	14102430	3
Caelo	Glucose monohydrate	4616M-02209	1
Caelo	Glucose monohydrate	17136805	12
Caelo	Glucose monohydrate	17005801	3
Caelo	Glucose monohydrate	14334805	2
Caelo	Glucose monohydrate	11314516	3
Caelo	Glucose monohydrate	15413304/20160309/6	1
Caelo	Glucose monohydrate	14334806	3
Caelo	Glucose monohydrate	15095606	1
Caelo	Glucose monohydrate	2017Q-02209	1
Caelo	Glucose monohydrate	19073310	1
Caelo	Glucose monohydrate	15180012	17
Caelo	Glucose monohydrate	15413302	3
Caelo	Glucose monohydrate	1518002	1
Caelo	Glucose monohydrate	18101902	5
Caelo	Glucose monohydrate	17005804	8
Caelo	Glucose monohydrate	18030004	6
Caelo	Glucose monohydrate	170058025621	1
Caelo	Glucose monohydrate	18101909	1
Caelo	Glucose monohydrate	16049105	9
Caelo	Glucose monohydrate	12G30-N01	1
Caelo	Glucose monohydrate	16049102	7
Caelo	Glucose monohydrate	13157026	3
Caelo	Glucose monohydrate	14102411	4
Caelo	Glucose monohydrate	11314528	8
Caelo	Glucose monohydrate	12284206	5
Caelo	Glucose monohydrate	12284219	8
Caelo	Glucose monohydrate	12284229	3
Caelo	Glucose monohydrate	13157005	12
Caelo	Glucose monohydrate	13157011	9
Caelo	Glucose monohydrate	13157012	1
Caelo	Glucose monohydrate	13157013	1
Caelo	Glucose monohydrate	14102424	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Glucose monohydrate	14334808	2
Caelo	Glucose monohydrate	14334809	1
Caelo	Glucose monohydrate	15413412	3
Caelo	Glucose monohydrate	1803006	1
Caelo	Glucose monohydrate	19073301	3
Caelo	Glucose monohydrate	17005802	11
Caelo	Glucose monohydrate	18214708	5
Caelo	Glucose monohydrate	18214710	3
Caelo	Glucose monohydrate	170100401	1
Caelo	Glucose monohydrate	1707004-01	5
Caelo	Glucose monohydrate	12284222	3
Caelo	Glucose monohydrate	13H06-N08	2
Caelo	Glucose monohydrate	14B04-B01-291137	1
Caelo	Glucose monohydrate	5092	1
Caelo	Glucose monohydrate	15095603	1
Caelo	Glucose monohydrate	15413401	5
Caelo	Glucose monohydrate	15413402	6
Caelo	Glucose monohydrate	15413405	5
Caelo	Glucose monohydrate	123456	1
Caelo	Glucose monohydrate	16049108	4
Caelo	Glucose monohydrate	1618401	2
Caelo	Glucose monohydrate	716I-02209	1
Caelo	Glucose monohydrate	17005813	7
Caelo	Glucose monohydrate	170323183	1
Caelo	Glucose monohydrate	17136804	14
Caelo	Glucose monohydrate	17305003	20
Caelo	Glucose monohydrate	1801009	1
Caelo	Glucose monohydrate	18030003	8
Caelo	Glucose monohydrate	18030005	5
Caelo	Glucose monohydrate	18101903	13
Caelo	Glucose monohydrate	18214704	12
Caelo	Glucose monohydrate	UIUJHJH	1
Caelo	Glucose monohydrate	14102412	9
Caelo	Glucose monohydrate	14334810	6
Caelo	Glucose monohydrate	19073302	2
Caelo	Glucose monohydrate	13A25-N01	5
Caelo	Glucose monohydrate	14102418	10
Caelo	Glucose monohydrate	14334802	10
Caelo	Glucose monohydrate	14I04-B08	4
Caelo	Glucose monohydrate	16049104	17
Caelo	Glucose monohydrate	16184801	16
Caelo	Glucose monohydrate	16184808	5
Caelo	Glucose monohydrate	17136802	12
Caelo	Glucose monohydrate	18030006	1
Caelo	Glucose monohydrate	18214701	14
Caelo	Glucose monohydrate	1810907	1
Caelo	Glucose monohydrate	1707004-001	1
Caelo	Glucose monohydrate	19073304	3
Caelo	Glucose monohydrate	16049101	18
Caelo	Glucose monohydrate	12284230	3
Caelo	Glucose monohydrate	13157007	6
Caelo	Glucose monohydrate	14102421	4
Caelo	Glucose monohydrate	1410019-02	1
Caelo	Glucose monohydrate	15180010	6
Caelo	Glucose monohydrate	15413304	25
Caelo	Glucose monohydrate	1049103	1
Caeolo/Noweda	Glucose monohydrate	15413301	1
Caeolo/Phönix	Glucose monohydrate	16184810	2
Caesa/Phoenix	Glucose monohydrate	15413304	1
Caesar & Lorenz	Glucose monohydrate	13157007	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Glucose monohydrate	15180013	1
Caesar & Loretz GmbH	Glucose monohydrate	15413402	1
Caesar & Loretz GmbH	Glucose monohydrate	17005802	1
Caesar & Loretz GmbH	Glucose monohydrate	18214708	3
Caesar & Loretz GmbH	Glucose monohydrate	18214703	1
Caesar & Loretz GmbH	Glucose monohydrate	19073303	5
Caesar & Loretz/ Caesar...	Glucose monohydrate	18030004	1
Caesar & Loretz/Noweda	Glucose monohydrate	16049102	1
Caesar & Loretz/Phönix	Glucose monohydrate	18101907	1
Calo	Glucose monohydrate	15180010	2
Cealo	Glucose monohydrate	13157017	1
Cealo	Glucose monohydrate	14102430	1
Cealo/ Noweda	Glucose monohydrate	15413412	1
Dermapharm	Glucose monohydrate	1601016-02	1
dextro energy	Glucose monohydrate	19050634	1
dextro energy	Glucose monohydrate	19016127	1
Dextro Energy	Glucose monohydrate	13171	1
dextro energy / Noweda	Glucose monohydrate	L1299	1
Dextro Energy GmbH/Gehe	Glucose monohydrate	L4163	2
Dextro Energy GmbH/Gehe	Glucose monohydrate	L4164	1
Dextro Energy GmbH/Gehe	Glucose monohydrate	L4274	1
Dextro Energy GmbH/Sana...	Glucose monohydrate	L1299	1
Dextro Energy GmbH	Glucose monohydrate	L4036	1
Dextro Energy GmbH	Glucose monohydrate	L4273	1
Dextro GmbH/Noweda	Glucose monohydrate	L5301	1
Dextro/Krieger/15.05.13	Glucose monohydrate	13092	1
dextroenergy	Glucose monohydrate	190161027	1
Eigenherstellung	Glucose monohydrate	30912HML01	1
Eigenherstellung	Glucose monohydrate	110912HML01	1
Eigenherstellung	Glucose monohydrate	120912HML02	1
Eigenherstellung	Glucose monohydrate	180213HJK01	1
Eigenherstellung	Glucose monohydrate	110913HJK02	1
Eigenherstellung	Glucose monohydrate	40615HJK01	1
Eigenherstellung	Glucose monohydrate	160915HML01	1
EuRho	Glucose monohydrate	1108061-01	2
EuRho	Glucose monohydrate	1108061-02	1
EuRho	Glucose monohydrate	2710Q-02209	1
EuRho	Glucose monohydrate	1204044-01	2
EuRho	Glucose monohydrate	151780	1
EuRho/GEHE	Glucose monohydrate	1410019-01	1
EuRho/Phoenix	Glucose monohydrate	140500401	1
EuRho/Phoenix	Glucose monohydrate	1604006-01	1
Eurho/Sanacorp	Glucose monohydrate	1108061-01	2
Euro OTC	Glucose monohydrate	20160405-04	1
Euro OTC	Glucose monohydrate	160400602	2
Euro OTC	Glucose monohydrate	1707004	1
Euro OTC	Glucose monohydrate	18070501	1
Euro OTC	Glucose monohydrate	1406212209	1
Euro OTC	Glucose monohydrate	1204044-02	4
Euro OTC	Glucose monohydrate	2023012-1	1
Euro OTC	Glucose monohydrate	1210034-01	9
Euro OTC	Glucose monohydrate	2313E-02209	1
Euro OTC	Glucose monohydrate	1305030-01	4
Euro OTC	Glucose monohydrate	1305030-02	5
Euro OTC	Glucose monohydrate	1103027-01	1
Euro OTC	Glucose monohydrate	140500401	1
Euro OTC	Glucose monohydrate	1509006-01	18
Euro OTC	Glucose monohydrate	1601016-02	4
Euro OTC	Glucose monohydrate	1701002-01	23
Euro OTC	Glucose monohydrate	1707004-01	51

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Glucose monohydrate	1701002-02	6
Euro OTC	Glucose monohydrate	170700401	1
Euro OTC	Glucose monohydrate	23051802	1
Euro OTC	Glucose monohydrate	E255L	1
Euro OTC	Glucose monohydrate	180700501	1
Euro OTC	Glucose monohydrate	180100941	1
Euro OTC	Glucose monohydrate	18070521	1
Euro OTC	Glucose monohydrate	18101901	2
Euro OTC	Glucose monohydrate	1607024-02	30
Euro OTC	Glucose monohydrate	16040060-01	1
Euro OTC	Glucose monohydrate	1509006-1	1
Euro OTC	Glucose monohydrate	150402801	1
Euro OTC	Glucose monohydrate	1204044-01	3
Euro OTC	Glucose monohydrate	31102013B	1
Euro OTC	Glucose monohydrate	140101901	1
Euro OTC	Glucose monohydrate	140500402	1
Euro OTC	Glucose monohydrate	1604006-01	23
Euro OTC	Glucose monohydrate	1801009_01	1
Euro OTC	Glucose monohydrate	E267X	1
Euro OTC	Glucose monohydrate	130503001	1
Euro OTC	Glucose monohydrate	15040281	1
Euro OTC	Glucose monohydrate	1607024	1
Euro OTC	Glucose monohydrate	E617K	1
Euro OTC	Glucose monohydrate	1707004-001	1
Euro OTC	Glucose monohydrate	1807005-01	28
Euro OTC	Glucose monohydrate	151780	1
Euro OTC	Glucose monohydrate	1811020-1	1
Euro OTC	Glucose monohydrate	96-01	1
Euro OTC	Glucose monohydrate	1114U2209	1
Euro OTC	Glucose monohydrate	2001006-01	1
Euro OTC	Glucose monohydrate	15095601	1
Euro OTC	Glucose monohydrate	190801241	1
Euro OTC	Glucose monohydrate	1210034-02	10
Euro OTC	Glucose monohydrate	1604006-02	27
Euro OTC	Glucose monohydrate	1405004-01	16
Euro OTC	Glucose monohydrate	1908012-01	4
Euro OTC	Glucose monohydrate	1811020-02	3
Euro OTC	Glucose monohydrate	140004-01	1
Euro OTC	Glucose monohydrate	14005004-02	1
Euro OTC	Glucose monohydrate	1410019-01	6
Euro OTC	Glucose monohydrate	150900601	1
Euro OTC	Glucose monohydrate	1811020-01	17
Euro OTC	Glucose monohydrate	190402901	1
Euro OTC	Glucose monohydrate	170704401	1
Euro OTC	Glucose monohydrate	160101601	2
Euro OTC	Glucose monohydrate	1607024-01	16
Euro OTC	Glucose monohydrate	1405004-02	4
Euro OTG/ AHD	Glucose monohydrate	1701002-01	1
Euro OTG/ AHD	Glucose monohydrate	1801009-01	1
Euro/ Sanacorp	Glucose monohydrate	1504028-01	1
Euro/Alliance Healthcare	Glucose monohydrate	1604006-01	1
Euro/Noweda	Glucose monohydrate	1604006-02	2
Euroo	Glucose monohydrate	1604006-01	1
Euro OTC	Glucose monohydrate	1108061-01	2
Euro OTC	Glucose monohydrate	2013U-02209	1
Euro OTC	Glucose monohydrate	1509006-02	4
Euro OTC	Glucose monohydrate	1601016-01	19
Euro OTC	Glucose monohydrate	1210034-03	1
Euro OTC	Glucose monohydrate	1807005-02	3
Euro OTC	Glucose monohydrate	15180010	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Glucose monohydrate	141001901	1
Euro OTC	Glucose monohydrate	1504028-01	14
Euro OTC	Glucose monohydrate	1504028-02	10
Euro OTC	Glucose monohydrate	17136801	1
Fagron	Glucose monohydrate	8G31-N09	1
Fagron	Glucose monohydrate	E524W	1
Fagron	Glucose monohydrate	12G30-N01	12
Fagron	Glucose monohydrate	151780-0004	1
Fagron	Glucose monohydrate	270313PML01	1
Fagron	Glucose monohydrate	13A25-N01	6
Fagron	Glucose monohydrate	12B09-N05	1
Fagron	Glucose monohydrate	13A_N01	1
Fagron	Glucose monohydrate	E571X	1
Fagron	Glucose monohydrate	13C25-N09	8
Fagron	Glucose monohydrate	4213Q-02209	1
Fagron	Glucose monohydrate	13h06-n08	1
Fagron	Glucose monohydrate	14B04-B01-291137	7
Fagron	Glucose monohydrate	14B04-B01-291143	2
Fagron	Glucose monohydrate	14b28-b02-291353	1
Fagron	Glucose monohydrate	15B01291137	1
Fagron	Glucose monohydrate	14I04-B08	1
Fagron	Glucose monohydrate	14B04-B01-291138	2
Fagron	Glucose monohydrate	14I04B8298602	1
Fagron	Glucose monohydrate	1521-B06-309508	1
Fagron	Glucose monohydrate	15A21-B06-309508	3
Fagron	Glucose monohydrate	1404-B08-298601	2
Fagron	Glucose monohydrate	14I04-808	1
Fagron	Glucose monohydrate	14104-B08-302707	1
Fagron	Glucose monohydrate	1404-B08-298604	1
Fagron	Glucose monohydrate	4562135	1
Fagron	Glucose monohydrate	14102420	1
Fagron	Glucose monohydrate	14D30-B06-294678	1
Fagron	Glucose monohydrate	14I04-B08-298601	1
Fagron	Glucose monohydrate	1401019-01	1
Fagron	Glucose monohydrate	17136805	1
Fagron	Glucose monohydrate	13B01-N03	5
Fagron	Glucose monohydrate	E0AJ5	1
Fagron	Glucose monohydrate	1509006-01	1
Fagron	Glucose monohydrate	13C25N09	2
Fagron	Glucose monohydrate	14I04-B08-298602	3
Fagron	Glucose monohydrate	14B28-B02-291353	11
Fagron	Glucose monohydrate	13H14-B06-289483	1
Fagron	Glucose monohydrate	13H06-N08	17
Fagron	Glucose monohydrate	3413E-02209	1
Fagron	Glucose monohydrate	E144C	1
Fagron	Glucose monohydrate	14B28-B02-291354	3
Fagron	Glucose monohydrate	1407-808-307707	1
Fagron	Glucose monohydrate	14B28-B02	2
Fargon	Glucose monohydrate	13C25-N09	1
Fargon	Glucose monohydrate	13A25-N01	1
Fiebig/ Dextropur	Glucose monohydrate	L7045	1
Fragon	Glucose monohydrate	13H06-N08	1
Frey+Lau GmbH	Glucose monohydrate	1601016-01	1
GATT-KOLLER/PHOENIX	Glucose monohydrate	243/02142614	1
GATT-KOLLER/PHOENIX	Glucose monohydrate	243/02141714	1
Gehe	Glucose monohydrate	13157026	2
Gehe	Glucose monohydrate	1707004-01	1
Gehe	Glucose monohydrate	18101907	1
Gehe	Glucose monohydrate	18214703	1
GEHE	Glucose monohydrate	1707004-01	1

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Supplier	Substance	Batch	Spectra
GEHE	Glucose monohydrate	17005803	1
GEHE	Glucose monohydrate	18030003	1
Euro OTC	Glucose monohydrate	1305030-02	1
Gutenberg-Apotheke	Glucose monohydrate	14B04-B01	1
Kehr	Glucose monohydrate	18101907	1
Caelo	Glucose monohydrate	11314526	1
Klosterring	Glucose monohydrate	17136802	1
Kyberg Experts	Glucose monohydrate	L9009	1
Noweda	Glucose monohydrate	1204044-01	2
Noweda	Glucose monohydrate	1210034	1
Noweda 10.02.2015	Glucose monohydrate	14334802	3
Noweda 10.032016	Glucose monohydrate	15413304	2
Noweda 30.07.2015	Glucose monohydrate	15095612	1
Caelo	Glucose monohydrate	15095602	1
Euro OTC	Glucose monohydrate	180100901	2
Euro OTC	Glucose monohydrate	180100-01	1
Ph.Eur.8.0	Glucose monohydrate	1401019-02	1
pharma gmbh	Glucose monohydrate	1401019-01	1
Phoenix	Glucose monohydrate	1707004-01	1
Phoenix	Glucose monohydrate	3242	1
Phoenix	Glucose monohydrate	3385	1
Phoenix/Cealo	Glucose monohydrate	17305004	1
Euro OTC	Glucose monohydrate	140101902	2
phönix	Glucose monohydrate	16049101	1
phönix	Glucose monohydrate	16049104	1
phönix	Glucose monohydrate	16184816	1
Phönix	Glucose monohydrate	1210334-02	1
Phönix	Glucose monohydrate	1401019-01	1
Euro OTC	Glucose monohydrate	160704-01	1
Euro OTC	Glucose monohydrate	1801009-01	51
Euro OTC	Glucose monohydrate	187005-001	1
Phönix Gotha	Glucose monohydrate	1401019-01	1
Phönix Gotha	Glucose monohydrate	1405004-02	1
Euro OTC	Glucose monohydrate	1904029-01	12
Euro OTC	Glucose monohydrate	16184807	1
Roquette Freres/AHD	Glucose monohydrate	12G30-N01	1
Roquette Lestrem FR/ No...	Glucose monohydrate	1210034-02	1
sana	Glucose monohydrate	15095601	2
sanacorp	Glucose monohydrate	13157026	1
Sanacorp	Glucose monohydrate	12284230	1
Sanacorp	Glucose monohydrate	14102430	1
Sanacorp	Glucose monohydrate	3/AKD100	1
Sanacorp	Glucose monohydrate	16184810	1
Sanacorp	Glucose monohydrate	1607024-01	1
Sanacorp	Glucose monohydrate	18101903	2
Sanacorp,30.03.17, 7,12EUR	Glucose monohydrate	16184810	1
Euro OTC	Glucose monohydrate	1410019-02	4
Sonnenberg-Apotheke	Glucose monohydrate	140500401	1
Euro OTC	Glucose monohydrate	1401019-01	15
Fagron	Glucose monohydrate	12G30-N01	2
Fagron	Glucose monohydrate	13A25-No1	1
Fagron	Glucose monohydrate	13A25-N01	2
Fagron	Glucose monohydrate	13A25-n01	1
Caelo	Glucose monohydrate		3
Caeolo / noweda	Glucose monohydrate		1
Fagron	Glucose monohydrate	11L19-N13	1
Fagron	Glucose monohydrate	14B04-B01	3
Fagron	Glucose monohydrate		1

- 109 629 spectra from 742 *Apo-Ident* customers from a total of 31 563 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glucose monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glucose monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	440	0	118 702
Type C	0	1612	6	109 629

The substance/substance group *Glucose monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.6364 %)
Type C	100.0000 % (> 99.8899 %)	99.6292 % (> 99.4438 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glucose monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Potassium tartrate hemihydrate	18.66	—
Aciclovir	50.77	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glucose monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20799	22538	2.17	36.71
21274	23006	1.48	30.08
21905	21905	0.00	34.40
22308	22308	0.00	32.79
22538	22538	0.00	36.47
23006	23006	0.00	31.71
23304	23304	0.00	35.12
23802	23802	0.00	26.55
24162	24162	0.00	18.66

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glutamic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20436-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glutamic acid; Acidum glutaminicum

Special notes

When selecting the *Glutamic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glutamic acid	4	2	2

Second-stage model

For differentiation of the substance/substance group *Glutamic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glutamic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Glutamic acid	L1405023-01	21720	60	20140627
Euro OTC	Glutamic acid	1604056	22562	40	20160523*
Euro OTC	Glutamic acid	1604056	24124	40	20180613*
Fagron	Glutamic acid	11I30-N02	20840	40	AR-15-FG-010446-02
Fagron	Glutamic acid	15G31-B08-311884	23599	40	20150817

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Glutamic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Glutamic acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Glutamic acid	L1211001-01	21282	40
Euro OTC	Glutamic acid	1907031	24788	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 1 *Apo-Ident* customers from 2 batches from the substance/substance group *Glutamic acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Glutamic acid	28071505	1
Fagron	Glutamic acid	3031502	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glutamic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glutamic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	2	0	111 245

The substance/substance group *Glutamic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glutamic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	22.76	–
Midazolam hydrochloride	64.54	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glutamic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22562	22562	0.00	51.23
20840	20840	0.00	49.34
21720	22562	7.67	51.46
23599	22562	4.38	52.55
24124	24124	0.00	50.15

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glutamine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 23150-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glutamine; Glutaminum; L-glutamine

Special notes

When selecting the *Glutamine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glutamine	3	3	1

Second-stage model

For differentiation of the substance/substance group *Glutamine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glutamine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Glutamine	1702007	23150	40	20170322*
Euro OTC	Glutamine	1706010	23543	40	20170802*
Fagron	Glutamine	17E05-B06-334869	23415	40	20170601
Fagron	Glutamine	17E05-B06-334869	23416	40	AR-17-FG-016178-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Glutamine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Glutamine*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Glutamine	1802010	23950	40
Euro OTC	Glutamine	1806001	24121	40
Euro OTC	Glutamine	1901009	24483	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Glutamine*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Glutamine	1706010-01	1

- 111 246 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glutamine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glutamine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	120	0	119 022
Type C	0	1	0	111 246

The substance/substance group *Glutamine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8911 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glutamine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium citrate tetrahydrate	25.84	—
Minoxidil	33.50	—
Heparin sodium	39.82	—
Levothyroxin sodium	42.35	—
Magnesium citrate	50.40	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glutamine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23150	23150	0.00	26.56
23415	23416	0.61	26.75
23416	23416	0.00	26.62
23543	23543	0.00	25.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glycine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20823-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glycine; Glycinum

Special notes

When selecting the *Glycine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glycine	9	5	6

Second-stage model

For differentiation of the substance/substance group *Glycine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glycine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Glycine	13157303	21687	60	20130625
Caelo	Glycine	14147006	21818	60	AR-16-FG-012263-01
Caelo	Glycine	15262518	23124	40	20150910
Caelo	Glycine	170265	23295	40	20170315*
Caelo	Glycine	173493	23834	40	20180117*
Euro OTC	Glycine	1402022-01	21284	40	20140328
Euro OTC	Glycine	1402022-01	21534	60	AR-15-FG-005430-01
Euro OTC	Glycine	1801005	23912	40	20180125*
Fagron	Glycine	12G13-N04	20823	40	1401163
Fagron	Glycine	13G09-N03	21276	40	20120711

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 10 reference samples from the substance/substance group *Glycine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 229 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Glycine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Glycine	191009	24507	40
Euro OTC	Glycine	1605035	22683	40
Euro OTC	Glycine	1704015	23387	40
Euro OTC	Glycine	1906006	24793	40
Euro OTC	Glycine	1911011	25103	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 4 *Apo-Ident* customers from 7 batches from the substance/substance group *Glycine*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Glycine	15262503	1
Caelo	Glycine	17026502	1
Caelo	Glycine	14147005	1
Caelo	Glycine	15262502	2
Caelo	Glycine	15262504	1
Euro OTC	Glycine	1801005-01	1
Caelo	Glycine	15262518	1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glycine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glycine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	456	4	110 229
Type B	0	200	0	118 942
Type C	0	7	1	111 239

The substance/substance group *Glycine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	99.1304 % (> 98.4783 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glycine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levocarnitine	34.17	–
Midazolam hydrochloride	60.89	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glycine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20823	20823	0.00	111.68
21276	20823	8.61	112.15
21818	21818	0.00	95.01
23124	20823	20.37	107.83
21284	23912	8.03	89.48
21534	21534	0.00	84.42
21687	21534	10.37	87.96
23834	23834	0.00	87.89
23912	23912	0.00	86.10
23295	23295	0.00	122.37

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Glycopyrronium bromide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 23076-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Glycopyrronium bromide; Glycopyrronii bromidum

Special notes

When selecting the *Glycopyrronium bromide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glycopyrronium bromide	3	1	0

Second-stage model

For differentiation of the substance/substance group *Glycopyrronium bromide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Glycopyrronium bromide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Glycopyrronium b...	16E09-B08-331027	23076	40	1707615
Fagron	Glycopyrronium b...	16E09-B08-331027	23077	40	20160530
Fagron	Glycopyrronium b...	18C30-B07-350744	24183	40	20180502
Fagron	Glycopyrronium b...	18G25-B01-356318	24575	40	20180907

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Glycopyrronium bromide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Glycopyrronium bromide*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Glycopyrronium bromide	17D28-B04-341606	23939	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Glycopyrronium bromide*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Glycopyrronium bromide	18C30-B07-350744	2

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Glycopyrronium bromide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Glycopyrronium bromide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	40	0	119 102
Type C	0	1	1	111 245

The substance/substance group *Glycopyrronium bromide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Glycopyrronium bromide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	25.44	—
Atropine sulfate	41.52	—
Betamethasone dipropionate, micronized	48.74	—
Dexamethasone acetate	56.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Glycopyrronium bromide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23076	23076	0.00	30.04
23077	23076	1.14	29.99
24183	23076	2.21	30.01
24575	23076	2.89	30.07

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Gramicidin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20203-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Gramicidin; Gramicidinum

Special notes

When selecting the *Gramicidin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Gramicidin	4	2	6

Second-stage model

For differentiation of the substance/substance group *Gramicidin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Gramicidin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Gramicidin	13J15-N02	21253	40	AR-15-FG-000813-01
Fagron	Gramicidin	17E09-B02-341211	23744	40	AR-18-FG-008970-02
Fagron	Gramicidin	18A19-B14-350428	24171	40	20180704
Fagron	Gramicidin	18L20-B01-358528	24571	40	20190320

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Gramicidin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 192 spectra of 4 reference samples from the substance/substance group *Gramicidin*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Gramicidin	14C07-B06-292886	21544	40
Fagron	Gramicidin	15H18-B01-316269	22748	40

continued on the next page

continued from previous page

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Gramicidin	13J15-N02	21253SI [†]	60
Fagron	Gramicidin	14C07-B06-292886	21544SI	52

- 118 950 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 5 *Apo-Ident* customers from 7 batches from the substance/substance group *Gramicidin*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Gramicidin	11F-24-N03	1
Fagron	Gramicidin	12K22-N12	1
Fagron	Gramicidin	B3200266	1
Fagron	Gramicidin	14H06-B03-297614	2
Fagron	Gramicidin	15H18B01316269	1
Fagron	Gramicidin	15C11-B04-306766	1
Fagron	Gramicidin	17E09-B02-341211	1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Gramicidin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Gramicidin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	122	70	118 950
Type C	0	8	0	111 239

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

The substance/substance group *Gramicidin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	63.5417 % (> 61.9792 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Gramicidin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisone	17.48	—
Prednisolone acetate	37.41	—
Polymyxin B sulfate	38.30	—
Triamcinolone, micronized	45.63	—
Cyanocobalamin	45.72	—
Magnesium citrate	46.31	—
Bacitracin	46.72	—
Tyrothricin	48.54	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Gramicidin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21253	21253	0.00	18.21
23744	23744	0.00	18.03
24171	23744	1.41	17.62
24571	21253	3.91	19.07

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at

least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Griseofulvin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20939-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Griseofulvin; Griseofulvinum

Special notes

When selecting the *Griseofulvin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Griseofulvin	3	2	51

Second-stage model

For differentiation of the substance/substance group *Griseofulvin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Griseofulvin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Griseofulvin	13D19-N03	20939	40	1401419
Fagron	Griseofulvin	14E16-B01-296834	21725	60	20140526
Fagron	Griseofulvin	16F13-B06-330832	23594	40	20160713

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Griseofulvin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Griseofulvin*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Griseofulvin	17L05-B05-345995	23996	40
Fagron	Griseofulvin	18L04_B01-357660	24440	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 98 spectra from 38 *Apo-Ident* customers from 56 batches from the substance/substance group *Griseofulvin*.
- Among them are spectra of independent samples from 51 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Griseofulvin	15B10-B06-306663	1
Bombastus	Griseofulvin	15L03-HH150640	1
Bombastus	Griseofulvin	16F13-B06-326073	1
Caelo	Griseofulvin	16F13-B06-323068	1
Caelo	Griseofulvin	16F13-B06-326074	1
Caelo	Griseofulvin	16F13-B06-330833	1
Caelo	Griseofulvin	100910	1
Euro OTC	Griseofulvin	14E16-B01-300367	1
Fagron	Griseofulvin	11J11-N13	1
Fagron	Griseofulvin	12F18-N04	1
Fagron	Griseofulvin	12D04-N12	1
Fagron	Griseofulvin	13F12-N22	1
Fagron	Griseofulvin	13L-13B08	1
Fagron	Griseofulvin	130922	2
Fagron	Griseofulvin	13L13-B08-290316	4
Fagron	Griseofulvin	13L13-B08	1
Fagron	Griseofulvin	15062015A	1
Fagron	Griseofulvin	140410	2
Fagron	Griseofulvin	15B10-B06-396547	1
Fagron	Griseofulvin	15810-B06	1
Fagron	Griseofulvin	14E16-B01-300367	1
Fagron	Griseofulvin	15L03-B315624	1
Fagron	Griseofulvin	16F13-B06	1
Fagron	Griseofulvin	16F13-B06-330833	4
Fagron	Griseofulvin	16F13B06330833	1
Fagron	Griseofulvin	17L05-B05-34999	1
Fagron	Griseofulvin	17L05-B05	5
Fagron	Griseofulvin	HH171022	1
Fagron	Griseofulvin	17L05-B05-351232	4
Fagron	Griseofulvin	17L05B05352461	2
Fagron	Griseofulvin	17-L05-352461	1
Fagron	Griseofulvin	17L005-B05-352461	1
Fagron	Griseofulvin	18L04-B01-357660	1
Fagron	Griseofulvin	17L05-B05-352461	1
Fagron	Griseofulvin	18L04-B01-357660	1
Fagron	Griseofulvin	16F13-B06-326073	1
Fagron	Griseofulvin	15B10-B06	1
Fagron	Griseofulvin	14E16-B01-300366	3
Fagron	Griseofulvin	15B10-B06-306547	9
Fagron	Griseofulvin	16f13-b06-330833	1
Fagron	Griseofulvin	17L05-B05-345995	1

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Supplier	Substance	Batch	Spectra
Fagron	Griseofulvin	18L04-B01-361614	1
Fagron	Griseofulvin	15103-b04-315624	1
Fagron	Griseofulvin	16f13-b06-326074	1
Fagron	Griseofulvin	17L05-B05	1
Fagron	Griseofulvin	10F03-N12	1
Fagron	Griseofulvin	13L13-B08-290317	1
Fagron	Griseofulvin	18L04-B01-359073	1
Fagron	Griseofulvin	18L04-B01-361615	1
Fagron	Griseofulvin	15L03-B04-315624	3
Fagron	Griseofulvin	18L04-B01	2
Fagron	Griseofulvin	HH160510	1
Fargon GmbH & Co.KG	Griseofulvin	16F13-B06-323067	1
Fargon/Sanacorp	Griseofulvin	17L05-B05-351231	1
Bombastus	Griseofulvin	17L05-B05-345996	1
Fagron	Griseofulvin	16F13-B06-323068	2
Fagron	Griseofulvin	16F13-B06-323067	2
Fagron	Griseofulvin	18L04-B01-357661	1
Noweda	Griseofulvin	16F13-B06-330833	1
Phönix Gotha	Griseofulvin	140410	1
Sanacorp	Griseofulvin	17L05-B05-345995	1
Sanacorp/ F	Griseofulvin	12B06-N07	1
Fagron	Griseofulvin	16F13-B06-330832	4
Fagron	Griseofulvin	13D19-N03	1

- 111 149 spectra from 742 *Apo-Ident* customers from a total of 31 835 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Griseofulvin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Griseofulvin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	81	17	111 149

The substance/substance group *Griseofulvin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	82.6531 % (> 79.5918 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Griseofulvin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ethyl hydrogen fumarate calcium	27.97	—
Omeprazole	52.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Griseofulvin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20939	20939	0.00	65.45
21725	20939	5.62	63.61
23594	20939	1.17	68.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Guaifenesin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20551-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Guaifenesin; Guaifenesinum

Special notes

When selecting the *Guaifenesin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Guaifenesin	6	9	9

Second-stage model

For differentiation of the substance/substance group *Guaifenesin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Guaifenesin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Guaifenesin	163333	23051	40	20161221*
Caelo	Guaifenesin	172496	23644	40	20171005*
Euro OTC	Guaifenesin	1212002-01	21287	40	20121214
Euro OTC	Guaifenesin	1506044	21864	60	20150708*
Euro OTC	Guaifenesin	1605005	22555	40	20160525*
Euro OTC	Guaifenesin	1910023	24941	40	20191114*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Guaifenesin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Guaifenesin*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Guaifenesin	190134	24518	40
Euro OTC	Guaifenesin	1701011	22993	40
Euro OTC	Guaifenesin	1706006	23551	40
Euro OTC	Guaifenesin	1710033	23741	40
Euro OTC	Guaifenesin	1802001	23949	40
Euro OTC	Guaifenesin	1804004	24076	40
Euro OTC	Guaifenesin	1809011	24316	40
Euro OTC	Guaifenesin	1901047	24474	40
Euro OTC	Guaifenesin	1906008	24801	40

- 118 782 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 7 *Apo-Ident* customers from 10 batches from the substance/substance group *Guaifenesin*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Guaifenesin	12277307	1
Caelo	Guaifenesin	12277311	1
Caelo	Guaifenesin	15F30-b06-317816	1
Caelo	Guaifenesin	1212002-01	1
Caelo	Guaifenesin	16135507	1
Caelo	Guaifenesin	18018302	1
Caelo	Guaifenesin	15302502	1
Euro OTC	Guaifenesin	1706006-01	2
Euro OTC	Guaifenesin	1804004-01	1
Phoenix 05.07.2014	Guaifenesin	1402023-01	2

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 881 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Guaifenesin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Guaifenesin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	360	0	118 782
Type C	0	12	0	111 235

The substance/substance group *Guaifenesin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Guaifenesin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	23.95	—
Serine	34.66	—
Levothyroxin sodium	43.16	—
Oxytetracycline hydrochloride	51.32	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Guaifenesin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21287	22555	8.46	55.82
21864	21864	0.00	54.86
22555	22555	0.00	53.82
23051	23051	0.00	55.21
23644	23644	0.00	55.55
24941	24941	0.00	55.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Heparin sodium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20638-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Heparin sodium; Heparinum natricum

Special notes

When selecting the *Heparin sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Heparin sodium	6	11	18

Second-stage model

For differentiation of the substance/substance group *Heparin sodium* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Heparin sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Heparin sodium	12050009-03	21294	40	AR-15-FG-007427-02
Euro OTC	Heparin sodium	1605022-01	22804	40	9699
Fagron	Heparin sodium	12H30-N07	20798	40	1404230
Fagron	Heparin sodium	12L20-B01-317990	22824	40	20130312
Yino Pharma	Heparin sodium	YN01011170904	23978	40	20180411*
Yino Pharma	Heparin sodium	YN01011170904	23979	40	20180411*
Yino Pharma	Heparin sodium	YN01011170502	23980	40	20180411*
Yino Pharma	Heparin sodium	YN01011170502	23981	40	20180411*
Yino Pharma	Heparin sodium	YN01011170904	24195	40	20180531*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 9 reference samples from the substance/substance group *Heparin sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 329 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 480 spectra of 12 reference samples from the substance/substance group *Heparin sodium*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Heparin sodium	16I26-B02-332108	23591	40
Yino Pharma	Heparin sodium	YN01011R1170803	23976	40
Yino Pharma	Heparin sodium	YN010111805002	24196	40
Yino Pharma	Heparin sodium	YN010121805010	24197	40
Yino Pharma	Heparin sodium	YN01011R11901002	24907	40
Yino Pharma	Heparin sodium	YN010111906005	24908	40
Yino Pharma	Heparin sodium	YN010111906006	24909	40
Yino Pharma	Heparin sodium	YN010111907007	24910	40
Yino Pharma	Heparin sodium	YN010111908008	24911	40
Yino Pharma	Heparin sodium	YN010121810018	24912	40
Yino Pharma	Heparin sodium	YN010111910009	24984	40
Yino Pharma	Heparin sodium	YN01011R1170803	23977	40

- 118 662 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 26 spectra from 14 *Apo-Ident* customers from 19 batches from the substance/substance group *Heparin sodium*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Heparin sodium	16I26-B02-327885	1
Euro OTC	Heparin sodium	1605022-02	2
Fagron	Heparin sodium	11190188SH	2
Fagron	Heparin sodium	14D09-B08-293944	2
Fagron	Heparin sodium	12G19-B02-313422	1
Fagron	Heparin sodium	15A20-B02-307307	1
Fagron	Heparin sodium	16I26-B02-332108	1
Fagron	Heparin sodium	16I26-B02	1
Fagron	Heparin sodium	18C21-B03-349501	1
Fagron	Heparin sodium	12I20-B01-323107	1
Fagron	Heparin sodium	17L06-B01-354811	1
Fagron	Heparin sodium	14D09-B08-307077	1
Fagron	Heparin sodium	16I26-B02-327885	1
Fagron	Heparin sodium	13G03-N13	3
Fiebig	Heparin sodium	16190116C0	1
Gatt-Koller	Heparin sodium	1901027	1
Fagron	Heparin sodium	12190453CQ	1
L31	Heparin sodium	16I26-B02-337593	1
Phoenix	Heparin sodium	5920101900	1
Fagron	Heparin sodium	12H30-N07	2

- 111 221 spectra from 742 *Apo-Ident* customers from a total of 31 872 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Heparin sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Heparin sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	480	0	118 662
Type C	0	26	0	111 221

The substance/substance group *Heparin sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.7500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 76.9231 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Heparin sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium citrate tetrahydrate	56.63	—
⋮	⋮	⋮
Dexamethasone	>50	99.75
Triamcinolone acetonide	>50	134.68
Triamcinolone, micronized	>50	140.58
Erythromycin	>50	168.58
Prednisolone, micronized	>50	177.34
Budesonide, micronized	>50	179.91
Prednicarbate, micronized	>50	207.64
Betamethasone valerate	>50	226.66

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Substanz	Distance in main model	Distance in second-stage model
Capsaicin	>50	256.75
Prednisone	>50	264.87
Betamethasone, micronized	>50	443.22
Norethisterone acetate	>50	493.65

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Heparin sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24195	24195	0.00	54.08
20798	20798	0.00	34.56
23981	23981	0.00	34.24
23978	23978	0.00	56.06
22824	21294	9.45	43.81
23979	23979	0.00	54.36
23980	23980	0.00	37.80
21294	21294	0.00	53.25
22804	22804	0.00	53.51

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Histamine dihydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20963-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Histamine dihydrochloride; Histamini dihydrochloridum

Special notes

When selecting the *Histamine dihydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Histamine dihydrochloride	4	3	23

Second-stage model

For differentiation of the substance/substance group *Histamine dihydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Histamine dihydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Histamine dihydr...	1111004-02	20963	40	1403674
Euro OTC	Histamine dihydr...	1506030	21863	60	20150706*
Fagron	Histamine dihydr...	14G16-B02-299175	21668	100	20140729
Fagron	Histamine dihydr...	19D19-B02-361228	24589	40	20190516

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 4 reference samples from the substance/substance group *Histamine dihydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Histamine dihydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Histamine dihydrochloride	1812018	24541	40
Euro OTC	Histamine dihydrochloride	1905003	24616	40
Fagron	Histamine dihydrochloride	15C25-B50-331242	23196	40
Fagron	Histamine dihydrochloride	15C25-B50-331242	23197	40

- 118 982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 46 spectra from 25 *Apo-Ident* customers from 25 batches from the substance/substance group *Histamine dihydrochloride*.
- Among them are spectra of independent samples from 23 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Histamine dihydrochloride	1111004-02	1
Caelo	Histamine dihydrochloride	130500601	1
Euro OTC	Histamine dihydrochloride	1104004-03	1
Euro OTC	Histamine dihydrochloride	20021412	1
Euro OTC	Histamine dihydrochloride	3031503	1
Euro OTC	Histamine dihydrochloride	1111004-01	5
Euro OTC	Histamine dihydrochloride	1905003-02	1
Euro OTC	Histamine dihydrochloride	1305006-01	1
Euro OTC	Histamine dihydrochloride	1411012-02	4
Euro OTC	Histamine dihydrochloride	1506030-01	3
Euro OTC	Histamine dihydrochloride	111004-02	1
Fa Roth	Histamine dihydrochloride	47252901	1
Fagron	Histamine dihydrochloride	12E29-N09	3
Fagron	Histamine dihydrochloride	11E25-N07	2
Fagron	Histamine dihydrochloride	12K06-N08	7
Fagron	Histamine dihydrochloride	28051305	1
Fagron	Histamine dihydrochloride	L17100130-0F-222030	1
Fagron	Histamine dihydrochloride	15E08-B06-313037	3
Fagron	Histamine dihydrochloride	454545	1
Fagron	Histamine dihydrochloride	12D02-N16	1
Fagron	Histamine dihydrochloride	14J06B01299179	1
Merck	Histamine dihydrochloride	Wxhc3407V	1
Merck	Histamine dihydrochloride	WXBC3407V	1
Sanacop	Histamine dihydrochloride	15C25-B01-306047	1
Euro OTC	Histamine dihydrochloride	1111004-02	1
Fagron	Histamine dihydrochloride	19D19-B02-361228	1

- 111 201 spectra from 742 *Apo-Ident* customers from a total of 31 867 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Histamine dihydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Histamine dihydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	160	0	118 982
Type C	0	46	0	111 201

The substance/substance group *Histamine dihydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 86.9565 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Histamine dihydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	32.73	—
L-threonine	51.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Histamine dihydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20963	20963	0.00	74.00
21668	20963	4.61	74.38
21863	21863	0.00	73.68
24589	21863	4.24	73.45

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Histidine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 23135-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Histidine; Histidinum; L-histidine

Special notes

When selecting the *Histidine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Histidine	3	1	0

Second-stage model

For differentiation of the substance/substance group *Histidine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Histidine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Histidine	1703022	23135	40	20170405*
Fagron	Histidine	15I01-B12-329082	23590	40	20150921
Fagron	Histidine	18J03-B02-355093	24701	40	20181123

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Histidine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Histidine*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Histidine	17F15-B04-343276	23935	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Histidine*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Histidine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Histidine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Histidine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Histidine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	59.31	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Histidine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24701	23135	5.32	109.20
23135	23135	0.00	106.51
23590	23135	5.60	109.05

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hyaluronic acid sodium salt**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21036-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hyaluronic acid sodium salt; Natrii Hyaluronas

Special notes

When selecting the *Hyaluronic acid sodium salt* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hyaluronic acid sodium salt	2	2	14

Second-stage model

For differentiation of the substance/substance group *Hyaluronic acid sodium salt* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hyaluronic acid sodium salt*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Hyaluronic acid ...	AP30101404H	22262	60	20141203
Audor Pharma	Hyaluronic acid ...	AP30101702H	23602	40	1802037

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 100 spectra of 2 reference samples from the substance/substance group *Hyaluronic acid sodium salt*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 589 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Hyaluronic acid sodium salt*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hyaluronic acid sodium salt	172347	23620	40
Euro OTC	Hyaluronic acid sodium salt	L1302028-01	21036	40
Euro OTC	Hyaluronic acid sodium salt	L1302028-01	21074	60

- 119 002 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 21 spectra from 12 *Apo-Ident* customers from 15 batches from the substance/substance group *Hyaluronic acid sodium salt*.
- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Hyaluronic acid sodium salt	AP30101305H	2
Audor Pharma	Hyaluronic acid sodium salt	AP30101505H	1
Caelo	Hyaluronic acid sodium salt	17234702	1
Caelo	Hyaluronic acid sodium salt	1263303	1
Caelo	Hyaluronic acid sodium salt	14364706	2
Caelo	Hyaluronic acid sodium salt	14188702	1
Caelo	Hyaluronic acid sodium salt	16246703	1
Caelo	Hyaluronic acid sodium salt	15204901	1
Caelo	Hyaluronic acid sodium salt	15204903	3
Caelo	Hyaluronic acid sodium salt	15448803	1
Caelo/AHD	Hyaluronic acid sodium salt	14364704	1
Euro OTC	Hyaluronic acid sodium salt	L1710023-02	1
Euro OTC	Hyaluronic acid sodium salt	L1512025-01	2
Fagron	Hyaluronic acid sodium salt	L1311012-01	1
Audor Pharma	Hyaluronic acid sodium salt	AP30101404H	2

- 111 226 spectra from 742 *Apo-Ident* customers from a total of 31 876 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hyaluronic acid sodium salt* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hyaluronic acid sodium salt* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	110 589
Type B	0	140	0	118 996
Type C	0	16	5	111 223

The substance/substance group *Hyaluronic acid sodium salt* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8898 %)	76.1905 % (> 61.9048 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hyaluronic acid sodium salt* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carmellose sodium (400 / 450 / 500 / 6...	25.79	—
SyrSpend [®] SF Alka	30.41	—
Acacia, dried dispersion	41.18	—
Rice starch	43.36	—
Aciclovir	45.87	—
Corn starch	48.26	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hyaluronic acid sodium salt* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22262	23602	16.80	29.80
23602	23602	0.00	25.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hydrochlorothiazide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20323-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hydrochlorothiazide; Hydrochlorothiazidum

Special notes

When selecting the *Hydrochlorothiazide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydrochlorothiazide	4	3	71

Second-stage model

For differentiation of the substance/substance group *Hydrochlorothiazide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hydrochlorothiazide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydrochlorothiaz...	13008505	21589	60	AR-15-FG-014461-01
Caelo	Hydrochlorothiaz...	182649	24362	40	20181127*
Fagron	Hydrochlorothiaz...	11L01-N02	20888	40	20111209
Fagron	Hydrochlorothiaz...	17L20-B02-345079	23989	40	20180125

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Hydrochlorothiazide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Hydrochlorothiazide*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydrochlorothiazide	14009701	23116	40
Caelo	Hydrochlorothiazide	192328	24888	40
Fagron	Hydrochlorothiazide	16F17-B07-327489	23600	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 201 spectra from 124 *Apo-Ident* customers from 75 batches from the substance/substance group *Hydrochlorothiazide*.
- Among them are spectra of independent samples from 71 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Hydrochlorothiazide	18017307	1
Caelo	Hydrochlorothiazide	13008507	1
Caelo	Hydrochlorothiazide	14B10-B01-294558	2
Caelo	Hydrochlorothiazide	14009701	21
Caelo	Hydrochlorothiazide	14B10-B01-305043	2
Caelo	Hydrochlorothiazide	15231002	3
Caelo	Hydrochlorothiazide	15231003	5
Caelo	Hydrochlorothiazide	15231005	1
Caelo	Hydrochlorothiazide	15231009	2
Caelo	Hydrochlorothiazide	16269301	4
Caelo	Hydrochlorothiazide	15231011	1
Caelo	Hydrochlorothiazide	16F17-B07-324062	1
Caelo	Hydrochlorothiazide	16269309	4
Caelo	Hydrochlorothiazide	18017303	1
Caelo	Hydrochlorothiazide	18017302	3
Caelo	Hydrochlorothiazide	16269312	1
Caelo	Hydrochlorothiazide	18017305	4
Caelo	Hydrochlorothiazide	18264901	4
Caelo	Hydrochlorothiazide	15231008	2
Caelo	Hydrochlorothiazide	16F17B07327489	1
Caelo	Hydrochlorothiazide	16269311	1
Caelo	Hydrochlorothiazide	18264904	1
Caelo	Hydrochlorothiazide	13008509	5
Caelo	Hydrochlorothiazide	16F17-B07-327489	1
Caelo	Hydrochlorothiazide	16269307	3
Caelo	Hydrochlorothiazide	16269313	2
Caelo	Hydrochlorothiazide	17H28-B01-340561	1
Caelo	Hydrochlorothiazide	18264907	1
Caelo	Hydrochlorothiazide	18017304	3
Caesar & Loretz GmbH	Hydrochlorothiazide	192328002	1
Fagron	Hydrochlorothiazide	11101-n02	2
Fagron	Hydrochlorothiazide	14B10-B01-294558	4
Fagron	Hydrochlorothiazide	11E04-N10	1
Fagron	Hydrochlorothiazide	2002311234	1
Fagron	Hydrochlorothiazide	11G12-N12	1

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Supplier	Substance	Batch	Spectra
Fagron	Hydrochlorothiazide	12L14-N11	4
Fagron	Hydrochlorothiazide	13C25-N08	6
Fagron	Hydrochlorothiazide	12A03-B40	3
Fagron	Hydrochlorothiazide	12A03-B40-286111	3
Fagron	Hydrochlorothiazide	12A03-B40-286110	1
Fagron	Hydrochlorothiazide	14b10-b01-294558	1
Fagron	Hydrochlorothiazide	13008504	1
Fagron	Hydrochlorothiazide	14B10-B01-300822	2
Fagron	Hydrochlorothiazide	14B10B01	1
Fagron	Hydrochlorothiazide	Co1-20150412	1
Fagron	Hydrochlorothiazide	15E04-B03	1
Fagron	Hydrochlorothiazide	15K16-B01-315836	2
Fagron	Hydrochlorothiazide	15K16	1
Fagron	Hydrochlorothiazide	16F17-B07-327489	5
Fagron	Hydrochlorothiazide	16F17-B07	2
Fagron	Hydrochlorothiazide	17H28-B01-340561	3
Fagron	Hydrochlorothiazide	17L20-B02-347789	4
Fagron	Hydrochlorothiazide	27101804	1
Fagron	Hydrochlorothiazide	17L20-B02-349593	3
Fagron	Hydrochlorothiazide	17L20-B02-353429	1
Fagron	Hydrochlorothiazide	CR0601	1
Fagron	Hydrochlorothiazide	CQ1108	1
Fagron	Hydrochlorothiazide	17L20B05	1
Fagron	Hydrochlorothiazide	12E04-N02	1
Fagron	Hydrochlorothiazide	14B10-B01-305043	2
Fagron	Hydrochlorothiazide	19A04-B01-363321	1
Fagron	Hydrochlorothiazide	5013Q-03660	1
Fagron	Hydrochlorothiazide	16F17-B07-324062	5
Fagron	Hydrochlorothiazide	C01-20150412	1
Fagron	Hydrochlorothiazide	15E04-B03-309670	5
Fagron	Hydrochlorothiazide	19A04-B01-359105	1
Fagron	Hydrochlorothiazide	17L20B02355636	1
Fagron	Hydrochlorothiazide	15K16-B01	2
Fagron	Hydrochlorothiazide	11Lo1-No2	1
Fiebig	Hydrochlorothiazide	115231003	1
Gehe	Hydrochlorothiazide	12E04-N02	1
Gehe	Hydrochlorothiazide	17L20-B02-353429	1
GEHE	Hydrochlorothiazide	18017302	1
Fagron	Hydrochlorothiazide	14B10-B01	2
Fagron	Hydrochlorothiazide	17L20-B02-355636	4
Noweda	Hydrochlorothiazide	16269307	1
Fagron	Hydrochlorothiazide	15K16-B01-319833	8
Phoenix	Hydrochlorothiazide	15231003	1
Phoenix	Hydrochlorothiazide	18017302	2
Phoenix	Hydrochlorothiazide	17L20-B02-347789	1
Phoenix	Hydrochlorothiazide	18264901	1
Phoenix	Hydrochlorothiazide	18264904	2
Caelo	Hydrochlorothiazide	16269304	2
Sanacorp	Hydrochlorothiazide	12A03-B40-26111	1
Sanacorp	Hydrochlorothiazide	15231008	1
Sanacorp	Hydrochlorothiazide	16269302	1
Sanacorp	Hydrochlorothiazide	18017302	1
Caelo	Hydrochlorothiazide	11101n02	1
Fagron	Hydrochlorothiazide	11L01-No2	1
Fagron	Hydrochlorothiazide	11L01-N02	2
Fagron	Hydrochlorothiazide	17L20-B02-345079	3

- 111 046 spectra from 742 *Apo-Ident* customers from a total of 31 816 batches from a further 706

substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hydrochlorothiazide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hydrochlorothiazide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	120	0	119 022
Type C	0	198	3	111 046

The substance/substance group *Hydrochlorothiazide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	98.5075 % (> 97.0149 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hydrochlorothiazide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	20.93	—
Sodium cromoglicate	37.08	—
Vancomycin hydrochloride	46.97	—
Oxytetracycline hydrochloride	56.60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hydrochlorothiazide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20888	21589	7.50	23.03
21589	21589	0.00	24.80
23989	24362	1.52	24.57
24362	24362	0.00	25.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hydrocortisone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20006-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hydrocortisone; Hydrocortisonum purum

Special notes

When selecting the *Hydrocortisone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydrocortisone	8	6	323

Second-stage model

For differentiation of the substance/substance group *Hydrocortisone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hydrocortisone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydrocortisone	13341502	21461	60	20131203
Caelo	Hydrocortisone	13341502	21463	60	20131203
Caelo	Hydrocortisone	180915	24020	40	20180412*
Euro OTC	Hydrocortisone	1206018-01	21293	40	20130727
Euro OTC	Hydrocortisone	1509029	21899	60	20151014*
Euro OTC	Hydrocortisone	1509029	21899SI	51	20151014*
Euro OTC	Hydrocortisone	1611016	22910	40	20161220*
Fagron	Hydrocortisone	16A19-B06-320970	22829	40	20160204
Fagron	Hydrocortisone	16A19-B06-320970	22829SI	30	20160204
Fagron	Hydrocortisone	16A19-B06-321981	22837	40	20160204
Fagron	Hydrocortisone	16A19-B06-321981	22838	40	1702302
Fagron	Hydrocortisone	16H01-B01-326071	22928	40	20160907
Fagron	Hydrocortisone	16H01-B01-326071	22928SI	40	20160907

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 581 spectra of 13 reference samples from the substance/substance group *Hydrocortisone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 108 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 719 spectra of 19 reference samples from the substance/substance group *Hydrocortisone*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydrocortisone	160952	22778	40
Caelo	Hydrocortisone	171194	23340	20
Caelo	Hydrocortisone	172566	23840	40
Caelo	Hydrocortisone	183243	24521	40
Euro OTC	Hydrocortisone	1802009	23945	40
Euro OTC	Hydrocortisone	1906033	24771	40
Caelo	Hydrocortisone	13341502	21463SI [†]	60
Caelo	Hydrocortisone	160952	22778SI	40
Caelo	Hydrocortisone	171194	23340SI	28
Caelo	Hydrocortisone	171194	23659	40
Caelo	Hydrocortisone	171194	23659SI	30
Caelo	Hydrocortisone	172566	23840SI	40
Caelo	Hydrocortisone	180915	24020SI [†]	40
Caelo	Hydrocortisone	183243	24521SI	40
Euro OTC	Hydrocortisone	1611016	22910SI [†]	40
Euro OTC	Hydrocortisone	1802009	23945SI	40
Euro OTC	Hydrocortisone	1906033	24771SI	40
Fagron	Hydrocortisone	16A19-B06-321981	22837SI [†]	30
Fagron	Hydrocortisone	16A19-B06-321981	22838SI [†]	31

- 118 423 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1849 spectra from 533 *Apo-Ident* customers from 337 batches from the substance/substance group *Hydrocortisone*.
- Among them are spectra of independent samples from 324 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
/ AHD	Hydrocortisone	16095202	1
A.H. 10.06.13 ek: 10,01EUR	Hydrocortisone	1204037-01	1
AHC 02.09.13 EK9,85	Hydrocortisone	1112030-01	1
AHD	Hydrocortisone	13069507	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
AHD	Hydrocortisone	18091503	1
AHD	Hydrocortisone	18091520	1
ahd,11,95EUR 10.04.14	Hydrocortisone	13341504-07R07	1
AHD;19.06.15;18,70EUR	Hydrocortisone	14301306	1
AHL	Hydrocortisone	15125-B01-313084	1
Fagron	Hydrocortisone	16J26-B04-330340	1
Caelo	Hydrocortisone	17256602	31
Alliance Health 11.01.2...	Hydrocortisone	1315505	1
Alliance Health25.04.2014	Hydrocortisone	13341503	3
Allianz Healthcare	Hydrocortisone	1509029-01	1
Anzag	Hydrocortisone	11260305	1
Anzag	Hydrocortisone	1107005-02	1
Anzag	Hydrocortisone	12104307	1
Anzag	Hydrocortisone	1206018-01	1
Anzag	Hydrocortisone	14301306	1
Anzag	Hydrocortisone	1501034-01	1
Anzag	Hydrocortisone	1505016-01	1
Anzag	Hydrocortisone	1509229-01	1
Anzag 14.12.12 ek:10,01	Hydrocortisone	1202032-01	1
Anzag ek:10.01EUR 18.07.12	Hydrocortisone	1107005-03	1
Caelo	Hydrocortisone	1518013	1
Beiersdorf/ Vedono	Hydrocortisone	15181004	1
Berkel AHK	Hydrocortisone	14301305	1
Bionorica	Hydrocortisone	16004604	1
Bombastus	Hydrocortisone	14I05-B02-300227	1
Caeelo	Hydrocortisone	17090005	1
Caelo	Hydrocortisone	15021107	11
Caelo	Hydrocortisone	2760	1
Caelo	Hydrocortisone	12104301	1
Caelo	Hydrocortisone	12104306	9
Caelo	Hydrocortisone	11273704	1
Caelo	Hydrocortisone	12104303	5
Caelo	Hydrocortisone	12119304	4
Caelo	Hydrocortisone	113I-01719	1
Caelo	Hydrocortisone	12119303	8
Caelo	Hydrocortisone	11021302	1
Caelo	Hydrocortisone	12104308	7
Caelo	Hydrocortisone	12167007	9
Caelo	Hydrocortisone	2013U-01719	1
Caelo	Hydrocortisone	12167010	10
Caelo	Hydrocortisone	10282208	1
Caelo	Hydrocortisone	13063501	1
Caelo	Hydrocortisone	7101301	1
Caelo	Hydrocortisone	13069506	8
Caelo	Hydrocortisone	21101303	1
Caelo	Hydrocortisone	810911	1
Caelo	Hydrocortisone	13069509	2
Caelo	Hydrocortisone	13069510	6
Caelo	Hydrocortisone	13155604	7
Caelo	Hydrocortisone	13155603	12
Caelo	Hydrocortisone	31032014D	1
Caelo	Hydrocortisone	13155605	3
Caelo	Hydrocortisone	13155614	3
Caelo	Hydrocortisone	13341511	3
Caelo	Hydrocortisone	14115107	11
Caelo	Hydrocortisone	14115105	3
Caelo	Hydrocortisone	14301305	5
Caelo	Hydrocortisone	14115103	2
Caelo	Hydrocortisone	14115104	1
Caelo	Hydrocortisone	14301310	13

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone	140301305	1
Caelo	Hydrocortisone	14301311	9
Caelo	Hydrocortisone	1501034-01	2
Caelo	Hydrocortisone	15021105	4
Caelo	Hydrocortisone	15021106	3
Caelo	Hydrocortisone	14301307	1
Caelo	Hydrocortisone	1505016-01	1
Caelo	Hydrocortisone	15181003	10
Caelo	Hydrocortisone	15181006	19
Caelo	Hydrocortisone	15181014	6
Caelo	Hydrocortisone	8717	1
Caelo	Hydrocortisone	15181007	5
Caelo	Hydrocortisone	15278703	8
Caelo	Hydrocortisone	15181012	14
Caelo	Hydrocortisone	260416v4	1
Caelo	Hydrocortisone	16004607	15
Caelo	Hydrocortisone	16004605	11
Caelo	Hydrocortisone	3081604	1
Caelo	Hydrocortisone	16004611	10
Caelo	Hydrocortisone	130617H	1
Caelo	Hydrocortisone	1518012	1
Caelo	Hydrocortisone	16095201	23
Caelo	Hydrocortisone	16004612	11
Caelo	Hydrocortisone	16095207	8
Caelo	Hydrocortisone	16272306	11
Caelo	Hydrocortisone	8041701	1
Caelo	Hydrocortisone	16255606	1
Caelo	Hydrocortisone	1611016-01	3
Caelo	Hydrocortisone	16272311	3
Caelo	Hydrocortisone	10071704	1
Caelo	Hydrocortisone	16255603	9
Caelo	Hydrocortisone	17119404	1
Caelo	Hydrocortisone	1672308	1
Caelo	Hydrocortisone	17119410	7
Caelo	Hydrocortisone	17090004	1
Caelo	Hydrocortisone	17119403	19
Caelo	Hydrocortisone	18121713	1
Caelo	Hydrocortisone	17256604	25
Caelo	Hydrocortisone	17256804	1
Caelo	Hydrocortisone	16041801	1
Caelo	Hydrocortisone	17351202	13
Caelo	Hydrocortisone	18042601	1
Caelo	Hydrocortisone	18061802	1
Caelo	Hydrocortisone	16255608NP	1
Caelo	Hydrocortisone	3110456	1
Caelo	Hydrocortisone	K05B20160909	1
Caelo	Hydrocortisone	1726603	1
Caelo	Hydrocortisone	1611016	1
Caelo	Hydrocortisone	27101801	1
Caelo	Hydrocortisone	16098201	2
Caelo	Hydrocortisone	1802009-01	1
Caelo	Hydrocortisone	18091506	14
Caelo	Hydrocortisone	18031508	1
Caelo	Hydrocortisone	18091528	4
Caelo	Hydrocortisone	18324301	7
Caelo	Hydrocortisone	18324308	3
Caelo	Hydrocortisone	18324311	2
Caelo	Hydrocortisone	15181012/20160309/10	1
Caelo	Hydrocortisone	12104304	6
Caelo	Hydrocortisone	17090005	8

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Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone	13155611	2
Caelo	Hydrocortisone	17351206	8
Caelo	Hydrocortisone	18091508	2
Caelo	Hydrocortisone	18091531	2
Caelo	Hydrocortisone	11260309	3
Caelo	Hydrocortisone	13155602	8
Caelo	Hydrocortisone	13342504	1
Caelo	Hydrocortisone	16095209	6
Caelo	Hydrocortisone	170921HA/17090003	1
Caelo	Hydrocortisone	18091501	17
Caelo	Hydrocortisone	18091524	7
Caelo	Hydrocortisone	18324302	2
Caelo	Hydrocortisone	4817Q-01719	1
Caelo	Hydrocortisone	15278702	9
Caelo	Hydrocortisone	16095213-20170704Ma7	1
Caelo	Hydrocortisone	17351209-20180830Ma3	1
Caelo	Hydrocortisone	18091501-H20181115Ma	3
Caelo	Hydrocortisone	18091505	17
Caelo	Hydrocortisone	15278706	6
Caelo	Hydrocortisone	13341503	1
Caelo	Hydrocortisone	14301313	5
Caelo	Hydrocortisone	18091525	16
Caelo	Hydrocortisone	14301312	7
Caelo	Hydrocortisone	12104305	3
Caelo	Hydrocortisone	13341508	4
Caelo	Hydrocortisone	16255604	2
Caelo	Hydrocortisone	17090003	4
Caelo	Hydrocortisone	1672305	1
Caelo	Hydrocortisone	15216101	7
Caelo	Hydrocortisone	167272306	1
Caelo	Hydrocortisone	18324306	2
Caelo	Hydrocortisone	12104309	2
Caelo	Hydrocortisone	1109845	1
Caelo	Hydrocortisone	13155601	9
Caelo	Hydrocortisone	17351209	11
Caelo	Hydrocortisone	3912Q-01719	1
Caelo	Hydrocortisone	12167001	7
Caelo	Hydrocortisone	120403701	1
Caelo	Hydrocortisone	14b04-B02-293422	1
Caelo	Hydrocortisone	17256603	8
Caelo	Hydrocortisone	1216707	1
Caelo	Hydrocortisone	13341504	7
Caelo	Hydrocortisone	13069502	5
Caelo	Hydrocortisone	15278705	11
Caelo	Hydrocortisone	17229410	1
Caelo	Hydrocortisone	1756602	1
Caelo	Hydrocortisone	18091507	14
Caelo	Hydrocortisone	18091502	2
Caelo	Hydrocortisone	18091520	12
Caelo	Hydrocortisone	18091519	16
Caelo	Hydrocortisone	13341510	11
Caelo	Hydrocortisone	16095210	19
Caelo	Hydrocortisone	16095212	6
Caelo	Hydrocortisone	11260308	3
Caelo	Hydrocortisone	15181004	10
Caelo	Hydrocortisone	1509029-01	2
Caelo	Hydrocortisone	16272305	9
Caelo	Hydrocortisone	16095213	10
Caelo	Hydrocortisone	16272304	12
Caelo	Hydrocortisone	16255680	1

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Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone	17119405	23
Caelo	Hydrocortisone	17256605	19
Caelo	Hydrocortisone	17256607	4
Caelo	Hydrocortisone	12104307	17
Caelo	Hydrocortisone	16004604	24
Caelo	Hydrocortisone	15/25-B01-318486	1
Caelo	Hydrocortisone	17119407	20
Caelo	Hydrocortisone	1719402-20171106Ma2	1
Caelo	Hydrocortisone	13069501	9
Caelo	Hydrocortisone	15021104	7
Caelo	Hydrocortisone	15181008	1
Caelo	Hydrocortisone	16004608	11
Caelo	Hydrocortisone	16255607	8
Caelo	Hydrocortisone	16255608	14
Caelo	Hydrocortisone	17119402	16
Caelo	Hydrocortisone	17119406	10
Caelo	Hydrocortisone	1626-B04-330340	1
Caelo	Hydrocortisone	17351205	42
Caelo	Hydrocortisone	18091503	16
Caelo	Hydrocortisone	12k08-n01	1
Caelo	Hydrocortisone	12167010-3437311151	1
Caelo	Hydrocortisone	13069505	4
Caelo	Hydrocortisone	13341509	8
Caelo	Hydrocortisone	14115108	2
Caelo	Hydrocortisone	16272308	4
Caelo	Hydrocortisone	16004603	11
Caelo	Hydrocortisone	1306906	1
Caeolo/Krieger	Hydrocortisone	17119406	1
Caesar & Loretz	Hydrocortisone	17256603	2
Caesar & Loretz GmbH	Hydrocortisone	12167010	1
Caesar & Loretz GmbH	Hydrocortisone	13069507	1
Caesar & Loretz GmbH	Hydrocortisone	13069506	1
Caesar & Loretz GmbH	Hydrocortisone	15021107	1
Caesar & Loretz GmbH	Hydrocortisone	15181012	1
Caesar & Loretz GmbH	Hydrocortisone	16004612	1
Caesar & Loretz GmbH	Hydrocortisone	17256605	1
Caesar & Loretz GmbH	Hydrocortisone	17351205	1
Caesar & Loretz GmbH	Hydrocortisone	18091506	2
Caesar & Loretz GmbH	Hydrocortisone	18091519	1
Caesar & Loretz GmbH	Hydrocortisone	17351210	2
Caesar & Loretz GmbH	Hydrocortisone	18091525	2
Caesar & Loretz GmbH	Hydrocortisone	18091526	1
Caesar & Loretz GmbH	Hydrocortisone	18324306	2
Caesar & Loretz GmbH	Hydrocortisone	18324307	1
Caesar & Loretz GmbH / ...	Hydrocortisone	18324306	1
Caesar & Loretz GmbH/Fi...	Hydrocortisone	18091508	1
Caesar & Loretz GmbH/Go...	Hydrocortisone	18324302	1
Caesar&Loretz GmbH	Hydrocortisone	12104308	1
Caesar&Loretz GmbH,Anza...	Hydrocortisone	16272305	1
Caesar&Loretz,Phoenix	Hydrocortisone	15021105	1
Caesar&Loretz,Phoenix	Hydrocortisone	15181004	1
Cealo	Hydrocortisone	17119405	1
Cealo/ Noweda	Hydrocortisone	17351209	1
Delta	Hydrocortisone	16H01-B01-326071	1
EuRho	Hydrocortisone	1107005-02	1
EuRho	Hydrocortisone	1405001-01	3
EuRho	Hydrocortisone	1202032-01	1
EuRho	Hydrocortisone	1509029-01	1
EuRho	Hydrocortisone	180200-01	1
EuRho 12.03.2013 Anzag	Hydrocortisone	1112030-01	1

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Supplier	Substance	Batch	Spectra
Eurho/ Phönix	Hydrocortisone	180200901	1
EURO / Gehe	Hydrocortisone	1405001-01	1
Euro OT/Anzag	Hydrocortisone	1611016-01	3
Euro OTC	Hydrocortisone	1107005-02	3
Euro OTC	Hydrocortisone	1112030-01	9
Euro OTC	Hydrocortisone	120403701	3
Euro OTC	Hydrocortisone	1408023-01	4
Euro OTC	Hydrocortisone	29011504	1
Euro OTC	Hydrocortisone	4091510	1
Euro OTC	Hydrocortisone	1509029-01	36
Euro OTC	Hydrocortisone	16272311	1
Euro OTC	Hydrocortisone	161016-01	1
Euro OTC	Hydrocortisone	17351202	1
Euro OTC	Hydrocortisone	1802008-01	1
Euro OTC	Hydrocortisone	17256603	1
Euro OTC	Hydrocortisone	1501034	1
Euro OTC	Hydrocortisone	1802009-01	38
Euro OTC	Hydrocortisone	1405001-01	2
Euro OTC	Hydrocortisone	157015	2
Euro OTC	Hydrocortisone	150902	1
Euro OTC	Hydrocortisone	161101601	2
Euro OTC	Hydrocortisone	180200901	2
Euro OTC	Hydrocortisone	210818A	1
Euro OTC	Hydrocortisone	1202032-01	3
Euro OTC	Hydrocortisone	1107005-01	1
Euro OTC	Hydrocortisone	1107005-03	8
Euro OTC	Hydrocortisone	3817A-01719	1
Euro OTC	Hydrocortisone	1204307-01	1
Euro OTC	Hydrocortisone	1501034-01	8
Euro OTC	Hydrocortisone	1611016-01	54
Euro OTC	Hydrocortisone	11611016-01	1
Euro OTC	Hydrocortisone	79(1802009-01)	1
Euro OTC	Hydrocortisone	80(1802009-01)	1
Euro OTC	Hydrocortisone	81(1802009-01)	1
Euro OTC	Hydrocortisone	82(1802009-01)	1
Euro OTC	Hydrocortisone	1505016-01	29
Euro OTC	Hydrocortisone	18091501	1
Euro OTC	Hydrocortisone	150501601	1
Euro OTC	Hydrocortisone	150929-01	1
Euro OTC	Hydrocortisone	181102182	1
Euro OTC	Hydrocortisone	715Q-01719	1
Euro OTC	Hydrocortisone	17119403	2
Euro OTC	Hydrocortisone	1204037-01	26
Euro OTC	Hydrocortisone	1906033-01	4
Euro/ Phönix	Hydrocortisone	1509029-01	1
Euro OTC	Hydrocortisone	6051502	1
Euro OTC	Hydrocortisone	12060018-01	1
Euro OTC	Hydrocortisone	16004612	1
Euro OTC	Hydrocortisone	15278703	1
Euro OTC	Hydrocortisone	4112A-01719	1
Euro OTC	Hydrocortisone	150516-01	1
Fagron	Hydrocortisone	18B21-B07-348432	1
Fagron	Hydrocortisone	12G19-N01	2
Fagron	Hydrocortisone	12/25-N01	1
Fagron	Hydrocortisone	12104304	1
Fagron	Hydrocortisone	12I25-N01	2
Fagron	Hydrocortisone	5061304	1
Fagron	Hydrocortisone	13H08-B01-285472	1
Fagron	Hydrocortisone	1204037-01	1
Fagron	Hydrocortisone	11021403	1

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Supplier	Substance	Batch	Spectra
Fagron	Hydrocortisone	13K22-B01-288284	3
Fagron	Hydrocortisone	120601801	1
Fagron	Hydrocortisone	19051403	1
Fagron	Hydrocortisone	K05B20130407M	1
Fagron	Hydrocortisone	12091401	1
Fagron	Hydrocortisone	14B04-B02-293423	3
Fagron	Hydrocortisone	K05B20131101	1
Fagron	Hydrocortisone	14B04-B02	2
Fagron	Hydrocortisone	14B04-B02-293424	6
Fagron	Hydrocortisone	14B04-B02-293422	3
Fagron	Hydrocortisone	14I05-B02-300228	1
Fagron	Hydrocortisone	14/05-B02-300227	2
Fagron	Hydrocortisone	13K22-B01-288282	1
Fagron	Hydrocortisone	14I05-B02-300229	1
Fagron	Hydrocortisone	14I05-B02	2
Fagron	Hydrocortisone	14/05-B02-300227	1
Fagron	Hydrocortisone	15/25-B01-318727	1
Fagron	Hydrocortisone	14I05-B02-300227	1
Fagron	Hydrocortisone	16H01-B01-324891	1
Fagron	Hydrocortisone	16j26-b04-330339	1
Fagron	Hydrocortisone	16H01-B01	1
Fagron	Hydrocortisone	17E10-B04-334857	5
Fagron	Hydrocortisone	17E10-B04	2
Fagron	Hydrocortisone	16272311	1
Fagron	Hydrocortisone	17E10-B04-334858	3
Fagron	Hydrocortisone	17E10-B04-336435	4
Fagron	Hydrocortisone	17351205	1
Fagron	Hydrocortisone	17/12-B05-344220	2
Fagron	Hydrocortisone	1712-B05-345540	1
Fagron	Hydrocortisone	17I12-B05	1
Fagron	Hydrocortisone	17-12B05-342611	1
Fagron	Hydrocortisone	16A19-B06	1
Fagron	Hydrocortisone	17E10-B04-335056	3
Fagron	Hydrocortisone	16A19-B06-321982	1
Fagron	Hydrocortisone	18B21-B07-348430	1
Fagron	Hydrocortisone	17E10-B04-335656	1
Fagron	Hydrocortisone	13341510	1
Fagron	Hydrocortisone	13H08-B01-285473	1
Fagron	Hydrocortisone	13H08-B01-285469	1
Fagron	Hydrocortisone	1509029-01	1
Fagron	Hydrocortisone	11K18-N01	2
Fagron	Hydrocortisone	15125-B01-318486	1
Fagron	Hydrocortisone	17C13-B06-333045	3
Fagron	Hydrocortisone	13K22-B01-288283	1
Fagron	Hydrocortisone	15D14-B02-311696	5
Fagron	Hydrocortisone	15I04-B03-315021	1
Fagron	Hydrocortisone	17/12-B05-344220	1
Fagron	Hydrocortisone	16H01-B01-324944	5
Fagron	Hydrocortisone	15/25-B01-313084	1
Fagron	Hydrocortisone	15D14-B02	1
Fagron	Hydrocortisone	18B21-B07-348431	1
Fagron	Hydrocortisone	17E10B04335656	1
Fagron	Hydrocortisone	17I12-B05-344220	1
Fagron	Hydrocortisone	17/12-b05-344220	1
Fagron	Hydrocortisone	17e10-b04-335056	1
Fagron	Hydrocortisone	12119303	1
Fagron	Hydrocortisone	17E-10-B04-334857	1
Fagron	Hydrocortisone	PH132	1
Fagron	Hydrocortisone	13H08B01285473	1
Fagron	Hydrocortisone	13H08-B01-28571	1

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Supplier	Substance	Batch	Spectra
Fagron	Hydrocortisone	14105-B02-300228	1
Fagron	Hydrocortisone	17256604	1
Fagron	Hydrocortisone	17112-B05-34554	1
Fagron	Hydrocortisone	18091501	1
Fagron	Hydrocortisone	K05M20170702	1
Fagron	Hydrocortisone	17G25-B02-340864	1
Fargo/Anzag	Hydrocortisone	17E10-B04-335056	1
Fargon	Hydrocortisone	17E10-B04-334858	1
fargon	Hydrocortisone	13K22-B01-288284	1
Fiebig	Hydrocortisone	1509029-01	2
Fiebig	Hydrocortisone	16095210	1
Fiebig	Hydrocortisone	16095207	1
Fiebig	Hydrocortisone	17119402	2
Fiebig	Hydrocortisone	17256602	1
Fiebig	Hydrocortisone	18091520	1
Fiebig	Hydrocortisone	18091525	1
Fiebig	Hydrocortisone	18091528	1
Caelo	Hydrocortisone	16095203	8
Finteler Apotheke	Hydrocortisone	1611016-01	3
Fragon/Sanacorp	Hydrocortisone	17E10-B04-335056	1
Gatt-Koller	Hydrocortisone	20172187	1
Gatt-Koller	Hydrocortisone	1804169	1
gehe	Hydrocortisone	16255607	1
Gehe	Hydrocortisone	12104304	3
Gehe	Hydrocortisone	13H08-B01-285471	1
Gehe	Hydrocortisone	13069510	1
Gehe	Hydrocortisone	13H08-B01-285469	1
Gehe	Hydrocortisone	1206018-01	2
Gehe	Hydrocortisone	1405001-01	1
Gehe	Hydrocortisone	1509029-01	1
Gehe	Hydrocortisone	16272306	1
Gehe	Hydrocortisone	16255607	1
Gehe	Hydrocortisone	17E10-B04-335656	1
Gehe	Hydrocortisone	17256604	1
Gehe	Hydrocortisone	18324301	2
GEHE	Hydrocortisone	16272311	1
GEHE	Hydrocortisone	18324301	1
Euro OTC	Hydrocortisone	1405001	1
Caelo	Hydrocortisone	16095202	11
GEHE 03.05.2014	Hydrocortisone	13155605	1
GEHE 14.04.2014	Hydrocortisone	13069509	1
Gehe,27.0415	Hydrocortisone	14301310	1
Caelo	Hydrocortisone	9271205	1
Caelo	Hydrocortisone	14301304	2
Caelo	Hydrocortisone	1140317	1
Caelo	Hydrocortisone	1190218/17256602	1
Gehe/Europharm	Hydrocortisone	1802009-01	1
Fagron	Hydrocortisone	17E10-B04-336436	2
Caelo	Hydrocortisone	133341502	1
Kehr	Hydrocortisone	16095213	1
Kehr	Hydrocortisone	17119407	1
Kehr	Hydrocortisone	17256602	1
Klenk	Hydrocortisone	12167007	1
L10	Hydrocortisone	16H01-B01-326071	2
L12	Hydrocortisone	1802009-01	1
Laborchemie Apolda/Phönix	Hydrocortisone	15181004	1
Midas	Hydrocortisone	17256602	1
Midas	Hydrocortisone	18091519	1
Nachprüfung 2312	Hydrocortisone	10282201	1
Noweda	Hydrocortisone	12104303	1

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Supplier	Substance	Batch	Spectra
Noweda	Hydrocortisone	12167001	1
Noweda	Hydrocortisone	13155605	1
Noweda	Hydrocortisone	16004612	1
Noweda	Hydrocortisone	16255608	1
Noweda	Hydrocortisone	1611016-01	1
Noweda 28.10.2019	Hydrocortisone	18091531	1
Caelo	Hydrocortisone	17526602	1
Euro OTC	Hydrocortisone	1505010601	1
Caelo	Hydrocortisone	18091526	2
Caelo	Hydrocortisone	18324310	1
Pharmachem/ Anzag	Hydrocortisone	18091520	1
Pharmacia&Upjohn/ Phönix	Hydrocortisone	13155614	1
Phoenix	Hydrocortisone	13341504	1
Phoenix	Hydrocortisone	1509029-01	2
Phoenix	Hydrocortisone	16095207	1
Phoenix	Hydrocortisone	1611016-01	1
Phoenix	Hydrocortisone	3117	1
Phoenix	Hydrocortisone	3370	1
Phoenix	Hydrocortisone	18324301	1
Phoenix	Hydrocortisone	18324306	1
Caelo	Hydrocortisone	16004612/2020317	1
phönix	Hydrocortisone	14301306	1
phönix	Hydrocortisone	15181013	1
Phönix	Hydrocortisone	11119-N03	1
Phönix	Hydrocortisone	12167001	2
Phönix	Hydrocortisone	12167010	1
Phönix	Hydrocortisone	1204037-01	1
Phönix	Hydrocortisone	13341504	2
Phönix	Hydrocortisone	13341508	1
Phönix	Hydrocortisone	1408023-01	1
Phönix	Hydrocortisone	1611016-01	2
Phönix	Hydrocortisone	3181	1
Phönix	Hydrocortisone	1802009-01	2
Phönix	Hydrocortisone	1906033	1
PHÖNIX	Hydrocortisone	17119410	1
Phönix 15.7.2019	Hydrocortisone	18091520	1
Phönix Caesar u. Loretz	Hydrocortisone	13225507	1
Phönix Gotha	Hydrocortisone	12104309	1
Phönix Gotha	Hydrocortisone	13341502	1
Phönix Gotha	Hydrocortisone	15181004	1
Phönix Gotha	Hydrocortisone	15021107	1
Caelo	Hydrocortisone	15181013	10
Caelo	Hydrocortisone	2180917/16255608	1
Caelo	Hydrocortisone	17351203	22
Euro OTC	Hydrocortisone	150902901	2
Sana	Hydrocortisone	18091524	3
sana corp	Hydrocortisone	13069507	1
sanacorp	Hydrocortisone	15181013	1
sanacorp	Hydrocortisone	15181012	1
Sanacorp	Hydrocortisone	1112030-01	1
Sanacorp	Hydrocortisone	13069509	1
Sanacorp	Hydrocortisone	13341509	1
Sanacorp	Hydrocortisone	42/AKD6	1
Sanacorp	Hydrocortisone	16004607	1
Sanacorp	Hydrocortisone	1509029-01	1
Sanacorp	Hydrocortisone	17256604	1
Caelo	Hydrocortisone	39/AKD17	1
Caelo	Hydrocortisone	13069507	4
Spangro 22.05.2014	Hydrocortisone	13341504	2
Spangro 23.1.2014	Hydrocortisone	13069510	1

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Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone	14301306	5
Spangro_21.05.2019	Hydrocortisone	18091524	1
Caelo	Hydrocortisone	13341501	7
Upjohn/Phönix	Hydrocortisone	1509029-01	1
VDL	Hydrocortisone	18091525	1
xxx	Hydrocortisone	911Q-01719	2
Caelo	Hydrocortisone	13341502	11
Caelo	Hydrocortisone		2
Euro OTC	Hydrocortisone	1206018-01	21
Euro OTC	Hydrocortisone	1509029	1
Euro OTC	Hydrocortisone	1611016	1
Fagron	Hydrocortisone		1
Fagron	Hydrocortisone	16A19-B06-321981	2
Fagron	Hydrocortisone	16A19-B06-320970	20
Fagron	Hydrocortisone	16H01-B01-326071	3
phönix	Hydrocortisone		2

- 109 398 spectra from 741 *Apo-Ident* customers from a total of 31 559 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hydrocortisone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hydrocortisone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	581	0	110 108
Type B	0	719	0	118 423
Type C	0	1736	113	109 398

The substance/substance group *Hydrocortisone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9673 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.1655 %)
Type C	100.0000 % (> 99.8899 %)	93.8886 % (> 93.7263 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hydrocortisone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methylcellulose	28.59	—
alpha-tocopheryl acetate dry concentrate	31.53	—
Hydroxypropylcellulose (300 mPa · s)	39.60	—
Menthol	40.68	—
Estradiol valerate	43.58	—
Escin, water-soluble	45.12	—
Povidone iodine	52.62	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hydrocortisone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22829	22838	5.96	45.13
22838	22838	0.00	43.14
21293	24020	2.80	44.17
21461	24020	3.83	40.77
21463	21899	2.21	39.60
21899	21899	0.00	40.77
22837	22838	2.26	44.89
22910	22910	0.00	40.49
22928	22910	2.07	39.28
24020	24020	0.00	44.11

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hydrocortisone acetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20010-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hydrocortisone acetate; Hydrocortisoni acetat

Special notes

When selecting the *Hydrocortisone acetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydrocortisone acetate	7	5	335

Second-stage model

For differentiation of the substance/substance group *Hydrocortisone acetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hydrocortisone acetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydrocortisone a...	13291708	21462	60	20130926
Caelo	Hydrocortisone a...	182780	24392	40	20181210*
Euro OTC	Hydrocortisone a...	1209003-01	21295	40	20121108
Euro OTC	Hydrocortisone a...	1209003-01	21295SI	45	20121108
Euro OTC	Hydrocortisone a...	1508029	21889	60	20150902*
Euro OTC	Hydrocortisone a...	1508029	21889SI	44	20150902*
Euro OTC	Hydrocortisone a...	1604052	22564	40	20160525*
Fagron	Hydrocortisone a...	15A30-B09-307090	22241	60	20150226
Fagron	Hydrocortisone a...	18H07-B03-356259	24590	40	20180829

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 429 spectra of 9 reference samples from the substance/substance group *Hydrocortisone acetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 260 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 451 spectra of 14 reference samples from the substance/substance group *Hydrocortisone acetate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydrocortisone acetate	16238706	23115	40
Caelo	Hydrocortisone acetate	170862	23328	40
Euro OTC	Hydrocortisone acetate	1706021	23559	40
Euro OTC	Hydrocortisone acetate	1805010	24130	40
Euro OTC	Hydrocortisone acetate	1907011	24789	40
Caelo	Hydrocortisone acetate	16238706	23115SI	20
Caelo	Hydrocortisone acetate	170862	23328SI	21
Caelo	Hydrocortisone acetate	182780	24392SI [†]	32
Euro OTC	Hydrocortisone acetate	1604052	22564SI [†]	30
Euro OTC	Hydrocortisone acetate	1706021	23559SI	30
Euro OTC	Hydrocortisone acetate	1805010	24130SI	21
Euro OTC	Hydrocortisone acetate	1907011	24789SI	40
Fagron	Hydrocortisone acetate	15A30-B09-307090	22241SI [†]	24
Fagron	Hydrocortisone acetate	18H07-B03-356259	24590SI [†]	33

- 118691 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2343 spectra from 584 *Apo-Ident* customers from 346 batches from the substance/substance group *Hydrocortisone acetate*.
- Among them are spectra of independent samples from 334 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone acetate	16238712	25
AEP	Hydrocortisone acetate	18278005	1
AEP	Hydrocortisone acetate	18278020	4
AHD	Hydrocortisone acetate	1205034-01	1
AHD	Hydrocortisone acetate	13291707	1
AHD	Hydrocortisone acetate	1706021-01	1
AHD 07.03.2017 EK: 5,33	Hydrocortisone acetate	16004407	1
Caelo	Hydrocortisone acetate	15356903	21
Caelo	Hydrocortisone acetate	1209003-01	6
Fagron	Hydrocortisone acetate	1604052-01	1
AHD;05,02,15; 12.48EUR	Hydrocortisone acetate	14144805	1
Alliance	Hydrocortisone acetate	1604052-01	1
Caelo	Hydrocortisone acetate	18278017	2
Caelo	Hydrocortisone acetate	12330108	15
Caelo	Hydrocortisone acetate	14301402	8

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Allianz	Hydrocortisone acetate	17219705	1
AMH Niemann/Sanacorp	Hydrocortisone acetate	17219705	1
Anzag	Hydrocortisone acetate	1112031-02	1
Anzag	Hydrocortisone acetate	1209003-01	1
Anzag	Hydrocortisone acetate	16238708	1
Anzag	Hydrocortisone acetate	16238712	1
Anzag	Hydrocortisone acetate	16238713	1
Anzag	Hydrocortisone acetate	17086206	2
Anzag	Hydrocortisone acetate	17219702	2
Anzag	Hydrocortisone acetate	17219703	1
Caelo	Hydrocortisone acetate	16004408	14
Fagron	Hydrocortisone acetate	1112031	1
Fagron	Hydrocortisone acetate	13J31B07290061	1
Apomix/Noweda	Hydrocortisone acetate	1404017-02	1
Bombastus	Hydrocortisone acetate	123Validierung	1
Bombastus	Hydrocortisone acetate	2712M01718	1
Bombastus	Hydrocortisone acetate	1604052-01	1
Bombastus	Hydrocortisone acetate	15356903	1
Caelo	Hydrocortisone acetate	17086204	1
Caelo/Anzag	Hydrocortisone acetate	15067003	1
Caelo	Hydrocortisone acetate	18278008	9
Caelo	Hydrocortisone acetate	1406211718	1
Caelo	Hydrocortisone acetate	15061207	1
Caelo	Hydrocortisone acetate	12008405	4
Caelo	Hydrocortisone acetate	11263905	1
Caelo	Hydrocortisone acetate	11098604	1
Caelo	Hydrocortisone acetate	11263913	1
Caelo	Hydrocortisone acetate	11263915	2
Caelo	Hydrocortisone acetate	11263917	3
Caelo	Hydrocortisone acetate	12008402	2
Caelo	Hydrocortisone acetate	12182403	5
Caelo	Hydrocortisone acetate	12182404	19
Caelo	Hydrocortisone acetate	12182402	10
Caelo	Hydrocortisone acetate	18011304	1
Caelo	Hydrocortisone acetate	12182405	17
Caelo	Hydrocortisone acetate	3110491	1
Caelo	Hydrocortisone acetate	2612M01718	1
Caelo	Hydrocortisone acetate	11263902	1
Caelo	Hydrocortisone acetate	1213M-01718	1
Caelo	Hydrocortisone acetate	12330106	4
Caelo	Hydrocortisone acetate	11098612	1
Caelo	Hydrocortisone acetate	7051303	1
Caelo	Hydrocortisone acetate	12330102	8
Caelo	Hydrocortisone acetate	12182408	2
Caelo	Hydrocortisone acetate	12330107	8
Caelo	Hydrocortisone acetate	12330110	2
Caelo	Hydrocortisone acetate	12330104	9
Caelo	Hydrocortisone acetate	12330112	13
Caelo	Hydrocortisone acetate	12330111	3
Caelo	Hydrocortisone acetate	12330116	10
Caelo	Hydrocortisone acetate	12330114	1
Caelo	Hydrocortisone acetate	27091307	1
Caelo	Hydrocortisone acetate	131553080	1
Caelo	Hydrocortisone acetate	17011402	1
Caelo	Hydrocortisone acetate	25101201	1
Caelo	Hydrocortisone acetate	12330113	1
Caelo	Hydrocortisone acetate	13155306	5
Caelo	Hydrocortisone acetate	13291704	3
Caelo	Hydrocortisone acetate	3110516	1
Caelo	Hydrocortisone acetate	2061401	1

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Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone acetate	1403903	1
Caelo	Hydrocortisone acetate	13291701	1
Caelo	Hydrocortisone acetate	14043906	9
Caelo	Hydrocortisone acetate	14043902	9
Caelo	Hydrocortisone acetate	27091403	1
Caelo	Hydrocortisone acetate	14043905	10
Caelo	Hydrocortisone acetate	14144805	21
Caelo	Hydrocortisone acetate	14043908	1
Caelo	Hydrocortisone acetate	14144804	4
Caelo	Hydrocortisone acetate	12021502	1
Caelo	Hydrocortisone acetate	14144802	1
Caelo	Hydrocortisone acetate	1501035	1
Caelo	Hydrocortisone acetate	14301408	8
Caelo	Hydrocortisone acetate	14301404	6
Caelo	Hydrocortisone acetate	28071508	1
Caelo	Hydrocortisone acetate	14301403	4
Caelo	Hydrocortisone acetate	15067005	18
Caelo	Hydrocortisone acetate	15067010	3
Caelo	Hydrocortisone acetate	15067006	11
Caelo	Hydrocortisone acetate	2734	1
Caelo	Hydrocortisone acetate	15356902	19
Caelo	Hydrocortisone acetate	15216204	2
Caelo	Hydrocortisone acetate	1505008-01	2
Caelo	Hydrocortisone acetate	1430140	1
Caelo	Hydrocortisone acetate	1536902	1
Caelo	Hydrocortisone acetate	16004406	18
Caelo	Hydrocortisone acetate	1600406	1
Caelo	Hydrocortisone acetate	160629HA	1
Caelo	Hydrocortisone acetate	160044402	1
Caelo	Hydrocortisone acetate	16095406	22
Caelo	Hydrocortisone acetate	15H24_B01-316480	1
Caelo	Hydrocortisone acetate	16238704	5
Caelo	Hydrocortisone acetate	16238708	22
Caelo	Hydrocortisone acetate	16238706	25
Caelo	Hydrocortisone acetate	16238705	3
Caelo	Hydrocortisone acetate	16238707	14
Caelo	Hydrocortisone acetate	16095402	1
Caelo	Hydrocortisone acetate	1623708	1
Caelo	Hydrocortisone acetate	1061704	1
Caelo	Hydrocortisone acetate	17086204	17
Caelo	Hydrocortisone acetate	6101707	1
Caelo	Hydrocortisone acetate	17086209	2
Caelo	Hydrocortisone acetate	163163055402	1
Caelo	Hydrocortisone acetate	17219704	19
Caelo	Hydrocortisone acetate	17219706	24
Caelo	Hydrocortisone acetate	18121710	1
Caelo	Hydrocortisone acetate	17219705	37
Caelo	Hydrocortisone acetate	17219710	1
Caelo	Hydrocortisone acetate	17219709	8
Caelo	Hydrocortisone acetate	2021803	1
Caelo	Hydrocortisone acetate	1605410	1
Caelo	Hydrocortisone acetate	172197085556	1
Caelo	Hydrocortisone acetate	18142802	12
Caelo	Hydrocortisone acetate	6071801	1
Caelo	Hydrocortisone acetate	18142805	21
Caelo	Hydrocortisone acetate	18142810	1
Caelo	Hydrocortisone acetate	17142802	1
Caelo	Hydrocortisone acetate	18142812	15
Caelo	Hydrocortisone acetate	12121801	1
Caelo	Hydrocortisone acetate	18142804	16

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone acetate	18142815	10
Caelo	Hydrocortisone acetate	18278010	17
Caelo	Hydrocortisone acetate	17358404	1
Caelo	Hydrocortisone acetate	18278015	6
Caelo	Hydrocortisone acetate	18278019	5
Caelo	Hydrocortisone acetate	172197050	1
Caelo	Hydrocortisone acetate	16095404	27
Caelo	Hydrocortisone acetate	13291706	10
Caelo	Hydrocortisone acetate	16004407	18
Caelo	Hydrocortisone acetate	17358403	6
Caelo	Hydrocortisone acetate	14043904	14
Caelo	Hydrocortisone acetate	14301401	13
Caelo	Hydrocortisone acetate	16238709	8
Caelo	Hydrocortisone acetate	16C15-B04-321459	1
Caelo	Hydrocortisone acetate	13155308	8
Caelo	Hydrocortisone acetate	12330105	3
Caelo	Hydrocortisone acetate	test	1
Caelo	Hydrocortisone acetate	11098615	1
Caelo	Hydrocortisone acetate	15A07-B03-306545	1
Caelo	Hydrocortisone acetate	14144806	13
Caelo	Hydrocortisone acetate	13155304	5
Caelo	Hydrocortisone acetate	15067003	12
Caelo	Hydrocortisone acetate	17086212	2
Caelo	Hydrocortisone acetate	20160727Ma2	1
Caelo	Hydrocortisone acetate	18142805-H20181115Ma	1
Caelo	Hydrocortisone acetate	18278016	6
Caelo	Hydrocortisone acetate	18142811	6
Caelo	Hydrocortisone acetate	25(1805010-01)	1
Caelo	Hydrocortisone acetate	18278003	5
Caelo	Hydrocortisone acetate	15061006	1
Caelo	Hydrocortisone acetate	16238713-20170818Ma2	1
Caelo	Hydrocortisone acetate	13G09-N08	2
Caelo	Hydrocortisone acetate	15356904	8
Caelo	Hydrocortisone acetate	1604052-01	6
Caelo	Hydrocortisone acetate	170804HA/1604052-01	1
Caelo	Hydrocortisone acetate	18142809	9
Caelo	Hydrocortisone acetate	18278018	3
Caelo	Hydrocortisone acetate	1918304	1
Caelo	Hydrocortisone acetate	16004405	12
Caelo	Hydrocortisone acetate	17086206	7
Caelo	Hydrocortisone acetate	19138302	1
Caelo	Hydrocortisone acetate	17219708	31
Caelo	Hydrocortisone acetate	16238713	6
Caelo	Hydrocortisone acetate	17086207	3
Caelo	Hydrocortisone acetate	172197055662	1
Caelo	Hydrocortisone acetate	14144803	9
Caelo	Hydrocortisone acetate	13291711	7
Caelo	Hydrocortisone acetate	12330103	8
Caelo	Hydrocortisone acetate	15067013	11
Caelo	Hydrocortisone acetate	18278004	17
Caelo	Hydrocortisone acetate	1391704	1
Caelo	Hydrocortisone acetate	15356901	14
Caelo	Hydrocortisone acetate	14043907	13
Caelo	Hydrocortisone acetate	13155307	2
Caelo	Hydrocortisone acetate	15067004	20
Caelo	Hydrocortisone acetate	16095407	26
Caelo	Hydrocortisone acetate	17219714	1
Caelo	Hydrocortisone acetate	11263916	1
Caelo	Hydrocortisone acetate	12183403	1
Caelo	Hydrocortisone acetate	17219702	15

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Hydrocortisone acetate	18278006	15
Caelo	Hydrocortisone acetate	18278007	9
Caelo	Hydrocortisone acetate	16095410	4
Caelo	Hydrocortisone acetate	18142803	9
Caelo	Hydrocortisone acetate	17086205	14
Caelo	Hydrocortisone acetate	13155302	8
Caelo	Hydrocortisone acetate	13291709	4
Caelo	Hydrocortisone acetate	13291705	4
Caelo	Hydrocortisone acetate	1391706	1
Caelo	Hydrocortisone acetate	14301406	17
Caelo	Hydrocortisone acetate	15067011	8
Caelo	Hydrocortisone acetate	16238714	13
Caelo	Hydrocortisone acetate	1604052	1
Caelo	Hydrocortisone acetate	17053185	1
Caelo	Hydrocortisone acetate	171106HA/17086204	1
Caelo	Hydrocortisone acetate	181115181	1
Caelo	Hydrocortisone acetate	180219HA/17219707	1
Caelo	Hydrocortisone acetate	17219703	19
Caelo	Hydrocortisone acetate	17358402	1
Fagron	Hydrocortisone acetate	18142806	1
Caelo	Hydrocortisone acetate	17219707	32
Caelo	Hydrocortisone acetate	13291707	12
Caelo	Hydrocortisone acetate	16004403	9
Caelo	Hydrocortisone acetate	14043901	10
Caelo	Hydrocortisone acetate	17086205-20170818Ma3	1
Caelo	Hydrocortisone acetate	3434	1
Caelo	Hydrocortisone acetate	19138307	4
Caelo	Hydrocortisone acetate	19138308	1
Caelo	Hydrocortisone acetate	14144807	6
Caelo	Hydrocortisone acetate	1430102	1
Caelo	Hydrocortisone acetate	16004402	16
Caelo	Hydrocortisone acetate	15H24-B01-314236	2
Caelo	Hydrocortisone acetate	16095405	17
Caelo	Hydrocortisone acetate	16095408	3
Caelo	Hydrocortisone acetate	1706021-01	5
Caelo	Hydrocortisone acetate	Caelo	2
Caelo	Hydrocortisone acetate	17086221	1
Caelo	Hydrocortisone acetate	17219713	2
Caelo	Hydrocortisone acetate	18142808	9
Caelo	Hydrocortisone acetate	18278020	2
Caelo	Hydrocortisone acetate	1205034-01	3
Caelo	Hydrocortisone acetate	12330111-3507411061	1
Caelo	Hydrocortisone acetate	14301407	16
Caelo	Hydrocortisone acetate	17086211	4
Caelo	Hydrocortisone acetate	18278014	5
Caelo	Hydrocortisone acetate	13155303	9
Caelo	Hydrocortisone acetate	160044003	1
Caeol/Phoenix	Hydrocortisone acetate	16004402	1
Caeolo/Noweda	Hydrocortisone acetate	13155303	1
caesar	Hydrocortisone acetate	14301402	1
Caesar & Loretz	Hydrocortisone acetate	16095404	1
Caesar & Loretz	Hydrocortisone acetate	18142815	2
Caesar & Loretz GmbH	Hydrocortisone acetate	12182405	1
Caesar & Loretz GmbH	Hydrocortisone acetate	15067004	1
Caesar & Loretz GmbH	Hydrocortisone acetate	16004402	1
Caesar & Loretz GmbH	Hydrocortisone acetate	16095406	2
Caesar & Loretz GmbH	Hydrocortisone acetate	16095405	1
Caesar & Loretz GmbH	Hydrocortisone acetate	16004408	1
Caesar & Loretz GmbH	Hydrocortisone acetate	17219706	1
Caesar & Loretz GmbH	Hydrocortisone acetate	17219708	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Hydrocortisone acetate	18142804	1
Caesar & Loretz GmbH	Hydrocortisone acetate	18278004	4
Caesar & Loretz GmbH	Hydrocortisone acetate	18278006	3
Caesar & Loretz GmbH	Hydrocortisone acetate	18278003	3
Caesar & Loretz GmbH	Hydrocortisone acetate	18278005	2
Caesar & Loretz GmbH	Hydrocortisone acetate	18278016	2
Caesar & Loretz GmbH	Hydrocortisone acetate	18278010	1
Caesar & Loretz GmbH	Hydrocortisone acetate	18278008	1
Caesar & Loretz GmbH	Hydrocortisone acetate	18278018	2
Caesar & Loretz GmbH	Hydrocortisone acetate	18278015	1
Caesar & Loretz GmbH	Hydrocortisone acetate	19138303	1
Caesar & Loretz GmbH / ...	Hydrocortisone acetate	14144806	1
Caesar & Loretz GmbH / ...	Hydrocortisone acetate	18278014	1
Caesar & Loretz GmbH/Al...	Hydrocortisone acetate	19138307	1
Caesar & Loretz GmbH/K	Hydrocortisone acetate	18278015	1
Caesar & Loretz GmbH/Sa...	Hydrocortisone acetate	19138307	1
Caesar & Loretz/AHD	Hydrocortisone acetate	17219706	1
Caesar u Loretz	Hydrocortisone acetate	15067003	1
Caesar&Loretz GmbH,Phön...	Hydrocortisone acetate	16238708	1
Caesar&Loretz GmbH/AHD	Hydrocortisone acetate	15356903	1
Caesar&Loretz GmbH/Anzag	Hydrocortisone acetate	14301405	2
Caesar&loretz,Phoenix	Hydrocortisone acetate	12182405	1
Caesar&loretz,Phoenix	Hydrocortisone acetate	12330103	1
caesar&loretz,PHönix,1...	Hydrocortisone acetate	15067003	1
Caesar&LoretzGmbH, Phoe...	Hydrocortisone acetate	18278006	1
Caolo	Hydrocortisone acetate	17219707	2
Cealo	Hydrocortisone acetate	1706021-01	1
Cealo / Noweda	Hydrocortisone acetate	13291707	1
Cealo/Gehe	Hydrocortisone acetate	16095410	2
Eplus	Hydrocortisone acetate	17219708	1
Eurho	Hydrocortisone acetate	1706021-01	1
EuRho	Hydrocortisone acetate	1107004-03	1
EuRho	Hydrocortisone acetate	17086212	1
EuRho	Hydrocortisone acetate	1706021-01	1
EuRho	Hydrocortisone acetate	1805010-01	7
EuRho/Phoenix	Hydrocortisone acetate	1209003-01	1
Euro OT/Anzag	Hydrocortisone acetate	1706021-01	2
Euro OTC	Hydrocortisone acetate	1505008-01	52
Euro OTC	Hydrocortisone acetate	140900502	1
Euro OTC	Hydrocortisone acetate	180501001	6
Euro OTC	Hydrocortisone acetate	1205034-01	24
Euro OTC	Hydrocortisone acetate	120503401	3
Euro OTC	Hydrocortisone acetate	1404017-01	12
Euro OTC	Hydrocortisone acetate	1409005-02	4
Euro OTC	Hydrocortisone acetate	150103501	3
Euro OTC	Hydrocortisone acetate	14301406	1
Euro OTC	Hydrocortisone acetate	15356903	1
Euro OTC	Hydrocortisone acetate	1604052-01	69
Euro OTC	Hydrocortisone acetate	16004406	2
Euro OTC	Hydrocortisone acetate	16238707	1
Euro OTC	Hydrocortisone acetate	2604052-01	1
Euro OTC	Hydrocortisone acetate	1508029-02	4
Euro OTC	Hydrocortisone acetate	1706021-01	61
Euro OTC	Hydrocortisone acetate	1706021	1
Euro OTC	Hydrocortisone acetate	1805010-01	37
Euro OTC	Hydrocortisone acetate	18050101	1
Euro OTC	Hydrocortisone acetate	1505008	1
Euro OTC	Hydrocortisone acetate	1112031-01	11
Euro OTC	Hydrocortisone acetate	1107004-03	2
Euro OTC	Hydrocortisone acetate	120900301	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Hydrocortisone acetate	17086204	1
Euro OTC	Hydrocortisone acetate	1112031-02	3
Euro OTC	Hydrocortisone acetate	150500801	3
Euro OTC	Hydrocortisone acetate	508029-01	2
Euro OTC	Hydrocortisone acetate	1409005-01	13
Euro OTC	Hydrocortisone acetate	1501035-01	14
Euro OTC	Hydrocortisone acetate	1404017-02	6
Euro OTC	Hydrocortisone acetate	HCAZ11004K	1
Euro OTC	Hydrocortisone acetate	L68934	1
Euro OTC	Hydrocortisone acetate	170830HA/1706021-01	1
Euro OTC	Hydrocortisone acetate	1404017-03	1
Euro OTC	Hydrocortisone acetate	17219705	1
Euro OTC	Hydrocortisone acetate	17066021-01	1
Euro OTC	Hydrocortisone acetate	12090003-01	3
Euro OTC	Hydrocortisone acetate	1706021-0	1
Euro OTC	Hydrocortisone acetate	911I-01718	1
Euro OTC	Hydrocortisone acetate	1502000801	1
Euro OTC	Hydrocortisone acetate	EuroOTC	2
Euro OTC	Hydrocortisone acetate	150802901	1
Euro/ Sanacorp	Hydrocortisone acetate	1409005-01	1
Euro/Alliance Healthcare	Hydrocortisone acetate	1508029-01	1
Euro/Gehe	Hydrocortisone acetate	1404017-01	1
Euro/Phönix	Hydrocortisone acetate	1805010	1
Euro OTC	Hydrocortisone acetate	1508029-01	34
Euro OTC	Hydrocortisone acetate	170602101	1
Euro OTC	Hydrocortisone acetate	170602-01	1
Euro OTC	Hydrocortisone acetate	18142805	1
Europh-Gehe	Hydrocortisone acetate	1508029-01	1
EuRro/Anzag	Hydrocortisone acetate	1706021-01	2
Fagro/Gehe	Hydrocortisone acetate	15A07-B03_306545	1
Fagro/Noweda	Hydrocortisone acetate	18142804	1
Fagron	Hydrocortisone acetate	12K15-N04	6
Fagron	Hydrocortisone acetate	11/01-N05	1
Fagron	Hydrocortisone acetate	13A03-N04	4
Fagron	Hydrocortisone acetate	13B25-N04	2
Fagron	Hydrocortisone acetate	3613A-01718	1
Fagron	Hydrocortisone acetate	13E31-No2	1
Fagron	Hydrocortisone acetate	13E31-N02	3
Fagron	Hydrocortisone acetate	14043903	1
Fagron	Hydrocortisone acetate	NCEHAC130201	1
Fagron	Hydrocortisone acetate	13J31-B07	3
Fagron	Hydrocortisone acetate	14043906	1
Fagron	Hydrocortisone acetate	13J31-B07-290061	2
Fagron	Hydrocortisone acetate	HC0024	1
Fagron	Hydrocortisone acetate	14043905	1
Fagron	Hydrocortisone acetate	14A13-B04-294158	2
Fagron	Hydrocortisone acetate	14I16-B01-300292	2
Fagron	Hydrocortisone acetate	13F25-B05-300290	2
Fagron	Hydrocortisone acetate	14301402	1
Fagron	Hydrocortisone acetate	13/31-B07-290061	1
Fagron	Hydrocortisone acetate	15A03-B09-307133	1
Fagron	Hydrocortisone acetate	15A07-B03-306545	1
Fagron	Hydrocortisone acetate	15A03-B09-307300	1
Fagron	Hydrocortisone acetate	15H24-B01-314236	1
Fagron	Hydrocortisone acetate	15H24-B01	1
Fagron	Hydrocortisone acetate	15J28-B12-317771	1
Fagron	Hydrocortisone acetate	16004402	1
Fagron	Hydrocortisone acetate	15h24-b01-314236	1
Fagron	Hydrocortisone acetate	15J28-B12	1
Fagron	Hydrocortisone acetate	160405201	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Hydrocortisone acetate	17C10-B01-333961	1
Fagron	Hydrocortisone acetate	17C10	2
Fagron	Hydrocortisone acetate	17L19	2
Fagron	Hydrocortisone acetate	17L19-B04-348983	2
Fagron	Hydrocortisone acetate	17L19-B04-350448	1
Fagron	Hydrocortisone acetate	17L19-B04	1
Fagron	Hydrocortisone acetate	18278005	1
Fagron	Hydrocortisone acetate	17G03-B06-341304	1
Fagron	Hydrocortisone acetate	16H18-B04	1
Fagron	Hydrocortisone acetate	16J28-B05	1
Fagron	Hydrocortisone acetate	13155311	1
Fagron	Hydrocortisone acetate	8563642	1
Fagron	Hydrocortisone acetate	NCEHAC151101	1
Fagron	Hydrocortisone acetate	15067006	1
Fagron	Hydrocortisone acetate	12330107	1
Fagron	Hydrocortisone acetate	17C10-B01-335774	1
Fagron	Hydrocortisone acetate	18H07-B03-352228	3
Fagron	Hydrocortisone acetate	16J28-B05-330083	1
Fagron	Hydrocortisone acetate	M39171	1
Fagron	Hydrocortisone acetate	16C15-B04-321458	1
Fagron	Hydrocortisone acetate	17G03-B06-345375	3
Fagron	Hydrocortisone acetate	18H07-B03-357240	2
Fagron	Hydrocortisone acetate	15A30-B09-307133	4
Fagron	Hydrocortisone acetate	16J28-B51-333889	3
Fagron	Hydrocortisone acetate	17G03-B06-341305	1
Fagron	Hydrocortisone acetate	14A13-B04	1
Fagron	Hydrocortisone acetate	15H24-B01-316480	1
Fagron	Hydrocortisone acetate	17086211	3
Fagron	Hydrocortisone acetate	7C10-B01-333961	1
Fagron	Hydrocortisone acetate	14144804	1
Fagron	Hydrocortisone acetate	16H18-B04-327325	1
Fagron	Hydrocortisone acetate	13J31-B07-290062	2
Fagron	Hydrocortisone acetate	17L19B04345374	1
Fagron	Hydrocortisone acetate	13G09-N08	4
Fagron	Hydrocortisone acetate	16H18-B04-325093	2
Fiebig	Hydrocortisone acetate	1209003-01	1
Fiebig	Hydrocortisone acetate	16095404	2
Fiebig	Hydrocortisone acetate	1605410	1
Fiebig	Hydrocortisone acetate	17219702	2
Fiebig	Hydrocortisone acetate	17219703	1
Fiebig	Hydrocortisone acetate	18142803	1
Fiebig	Hydrocortisone acetate	18278010	1
Fiebig	Hydrocortisone acetate	18278006	1
Finteler Apotheke	Hydrocortisone acetate	1604052-01	2
Gatt-Koller	Hydrocortisone acetate	1734/05154415	1
Gatt-Koller	Hydrocortisone acetate	1802876	1
gehe	Hydrocortisone acetate	17219707	1
Gehe	Hydrocortisone acetate	1205034-01	1
Gehe	Hydrocortisone acetate	14043905	1
Gehe	Hydrocortisone acetate	1501035-01	1
Gehe	Hydrocortisone acetate	16004408	1
Gehe	Hydrocortisone acetate	16238710	1
Gehe	Hydrocortisone acetate	17219705	3
Gehe	Hydrocortisone acetate	18142812	2
Gehe	Hydrocortisone acetate	18278004	2
Gehe	Hydrocortisone acetate	18278010	1
GEHE	Hydrocortisone acetate	1604052-01	1
GEHE	Hydrocortisone acetate	16238712	1
GEHE	Hydrocortisone acetate	16238713	1
GEHE	Hydrocortisone acetate	1706021-01	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
GEHE	Hydrocortisone acetate	17219703	1
GEHE	Hydrocortisone acetate	18278020	1
GEHE 03.07.2014	Hydrocortisone acetate	14043903	1
Euro OTC	Hydrocortisone acetate	140900501	1
Caelo	Hydrocortisone acetate	301115	1
Caelo	Hydrocortisone acetate	166004407	1
Caelo	Hydrocortisone acetate	1130317	1
Caelo	Hydrocortisone acetate	17086203	15
Fagron	Hydrocortisone acetate	17C10-B01-333962	3
Fagron	Hydrocortisone acetate	17G03-B06-338750	1
Fagron	Hydrocortisone acetate	17G03-B06-341843	1
Caelo	Hydrocortisone acetate	170602101	1
Caelo	Hydrocortisone acetate	1112031-02	1
Caelo	Hydrocortisone acetate	16238710	18
Hedinger/Gehe	Hydrocortisone acetate	1112031-02	1
Hedinger/Sanacorp	Hydrocortisone acetate	1706021-01	2
Klenk	Hydrocortisone acetate	1/06021-01	1
Hepart	Hydrocortisone acetate	14144804	1
Caelo	Hydrocortisone acetate	18142806	21
Ichthyol GmbH/Noweda	Hydrocortisone acetate	17086205	1
Kehr	Hydrocortisone acetate	1706021-01	2
Caelo	Hydrocortisone acetate	18142807	3
Klenk	Hydrocortisone acetate	14301401	1
Klenk	Hydrocortisone acetate	1112031-01	1
Klenk	Hydrocortisone acetate	18142803	1
L10	Hydrocortisone acetate	1706021-01	5
Caelo	Hydrocortisone acetate	170856206	1
L12	Hydrocortisone acetate	1604052-01	3
Caelo	Hydrocortisone acetate	1508029-01	2
Lihua/phönix	Hydrocortisone acetate	K06A20140801M	1
Midas	Hydrocortisone acetate	17219707	1
Noweda	Hydrocortisone acetate	1112031-02	1
Noweda	Hydrocortisone acetate	13G09-N08	1
Noweda	Hydrocortisone acetate	16095407	1
Noweda	Hydrocortisone acetate	17219706	1
Noweda	Hydrocortisone acetate	17219707	2
Noweda	Hydrocortisone acetate	18142804	2
Noweda	Hydrocortisone acetate	18278004	1
Noweda	Hydrocortisone acetate	18278014	1
Noweda	Hydrocortisone acetate	18278015	1
Noweda 17.07.2015	Hydrocortisone acetate	14301403	1
Noweda am 10.10.2017	Hydrocortisone acetate	1706021	1
Noweda/ Pharmacia & Upj...	Hydrocortisone acetate	1205034-01	1
Noweda/Apomix	Hydrocortisone acetate	16095407	1
Caelo	Hydrocortisone acetate	14301405	24
Caelo	Hydrocortisone acetate	16004404	1
Noweda/Euro	Hydrocortisone acetate	1501035-01	1
Euro OTC	Hydrocortisone acetate	160405201	5
Euro OTC	Hydrocortisone acetate	17086203	1
Euro OTC	Hydrocortisone acetate	17219709	1
Pharmacia&Upjohn Comp. ...	Hydrocortisone acetate	1209003-01	1
Phoenix	Hydrocortisone acetate	12182402	1
Phoenix	Hydrocortisone acetate	12330107	1
Phoenix	Hydrocortisone acetate	1568/05131813	1
Phoenix	Hydrocortisone acetate	1209003-01	1
Phoenix	Hydrocortisone acetate	15A30-B09	1
Phoenix	Hydrocortisone acetate	16004403	1
Phoenix	Hydrocortisone acetate	15J28-B12	1
Phoenix	Hydrocortisone acetate	3068	1
Phoenix	Hydrocortisone acetate	3209	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Phoenix	Hydrocortisone acetate	18142802	1
Phoenix	Hydrocortisone acetate	18H07-B03-352227	1
Phoenix	Hydrocortisone acetate	18278015	1
Phoenix 14.01.2015 EK: ...	Hydrocortisone acetate	14043902	1
Phoenix 24.01.2019	Hydrocortisone acetate	18278004	1
Phoenix Goettin	Hydrocortisone acetate	1209003-01	1
phönix	Hydrocortisone acetate	15356901	2
phönix	Hydrocortisone acetate	16238708	1
phönix	Hydrocortisone acetate	16238712	1
Phönix	Hydrocortisone acetate	12A13-N02	1
Phönix	Hydrocortisone acetate	1112031-01	1
Phönix	Hydrocortisone acetate	12K15-No4	1
Phönix	Hydrocortisone acetate	AKD8	1
Phönix	Hydrocortisone acetate	1205034-01	1
Phönix	Hydrocortisone acetate	1112031-02	1
Phönix	Hydrocortisone acetate	12182405	1
Phönix	Hydrocortisone acetate	14144804	1
Phönix	Hydrocortisone acetate	18278014	1
PHÖNIX	Hydrocortisone acetate	17086211	1
Phönix Gotha	Hydrocortisone acetate	12182405	1
Phönix Gotha	Hydrocortisone acetate	12330108	1
Caelo	Hydrocortisone acetate	18278005	18
Phönix/Lihua	Hydrocortisone acetate	1409005-01	1
sanacorp	Hydrocortisone acetate	14301406	1
Sanacorp	Hydrocortisone acetate	1107004-03	1
Sanacorp	Hydrocortisone acetate	11263913	1
Sanacorp	Hydrocortisone acetate	12182404	2
Sanacorp	Hydrocortisone acetate	12330103	1
Sanacorp	Hydrocortisone acetate	13155302	2
Sanacorp	Hydrocortisone acetate	13291704	1
Sanacorp	Hydrocortisone acetate	14043903	1
Sanacorp	Hydrocortisone acetate	1409005-01	3
Sanacorp	Hydrocortisone acetate	1501035-01	1
Sanacorp	Hydrocortisone acetate	16238706	1
Sanacorp	Hydrocortisone acetate	16238710	1
Sanacorp	Hydrocortisone acetate	16238708	1
Sanacorp	Hydrocortisone acetate	17219704	1
Sanacorp	Hydrocortisone acetate	18278006	1
Sanacorp	Hydrocortisone acetate	18278008	1
Caelo	Hydrocortisone acetate	10301904	1
Caelo	Hydrocortisone acetate	14043903	11
Euro OTC	Hydrocortisone acetate	1508023-01	1
SanacorpWE:13.02.2017 ...	Hydrocortisone acetate	1604052-01	1
	Hydrocortisone acetate	14043902	1
Caelo	Hydrocortisone acetate	13291708	7
Caelo	Hydrocortisone acetate		6
Euro OTC	Hydrocortisone acetate	1209003-01	20
Euro OTC	Hydrocortisone acetate	1508029	2
	Hydrocortisone acetate	333961	1
Fagron	Hydrocortisone acetate	18H07-B03-356259	1
Nachprüfung	Hydrocortisone acetate		1
xxx	Hydrocortisone acetate		1

- 108 904 spectra from 742 *Apo-Ident* customers from a total of 31 557 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hydrocortisone acetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hydrocortisone acetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	429	0	110 260
Type B	0	447	4	118 691
Type C	0	2236	107	108 904

The substance/substance group *Hydrocortisone acetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6014 %)
Type B	100.0000 % (> 99.9893 %)	99.1131 % (> 98.4479 %)
Type C	100.0000 % (> 99.8899 %)	95.4332 % (> 95.3052 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hydrocortisone acetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	38.15	—
Glycyrrhizic acid	40.27	—
Hydrocortisone	40.47	—
Escin, water-soluble	40.88	—
Cyanocobalamin	48.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hydrocortisone acetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21295	21889	4.15	39.56
21462	21889	4.39	39.57
21889	21889	0.00	39.01
22241	21889	3.17	40.16
24392	24392	0.00	39.58
24590	21889	2.89	38.15
22564	22564	0.00	39.59

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hydroquinone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20091-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hydroquinone; Hydrochinonum

Special notes

When selecting the *Hydroquinone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydroquinone	8	2	60

Second-stage model

For differentiation of the substance/substance group *Hydroquinone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hydroquinone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydroquinone	12288505	20884	40	20121015
Caelo	Hydroquinone	14026904	21468	60	20140122
Caelo	Hydroquinone	14281501	21791	60	AR-15-FG-008058-01
Caelo	Hydroquinone	14280110	21923	60	20141017
Caelo	Hydroquinone	15057004	21975	60	20150306
Caelo	Hydroquinone	15057001	22324	60	20150306
Caelo	Hydroquinone	15057001	22351	60	20150306
Caelo	Hydroquinone	182306	24761	40	20181008*
Caelo	Hydroquinone	192642	24890	40	20191115*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 480 spectra of 9 reference samples from the substance/substance group *Hydroquinone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 209 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Hydroquinone*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydroquinone	16023105	23114	40
Caelo	Hydroquinone	172215	23654	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 277 spectra from 181 *Apo-Ident* customers from 69 batches from the substance/substance group *Hydroquinone*.
- Among them are spectra of independent samples from 60 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
14026902	Hydroquinone	InterneCharge1214Q	1
16023112	Hydroquinone	16023112	1
A.H. 14.06.13 ek: 3,97EUR	Hydroquinone	12288505	1
ACM	Hydroquinone	KNC1047J15	2
ACM	Hydroquinone	KNC0635J17	1
AHD	Hydroquinone	13105405	1
AHL	Hydroquinone	16023102	1
Caelo	Hydroquinone	16023112	10
Allianz	Hydroquinone	16023116	1
Anzag	Hydroquinone	12156705	1
Anzag	Hydroquinone	12288505	2
Apomix/Noweda	Hydroquinone	13105408	1
Caelo	Hydroquinone	1163902	1
Caelo	Hydroquinone	11163907	5
Caelo	Hydroquinone	11163905	4
Caelo	Hydroquinone	10145103	1
Caelo	Hydroquinone	12156705	5
Caelo	Hydroquinone	14121202	1
Caelo	Hydroquinone	20200712-3	1
Caelo	Hydroquinone	1263912	1
Caelo	Hydroquinone	12156706	1
Caelo	Hydroquinone	12156703	1
Caelo	Hydroquinone	12288503	2
Caelo	Hydroquinone	13105402	4
Caelo	Hydroquinone	11163912/Int312052	1
Caelo	Hydroquinone	18031403	1
Caelo	Hydroquinone	14026902	5
Caelo	Hydroquinone	14180401	3
Caelo	Hydroquinone	21102014A	1
Caelo	Hydroquinone	14180410	4
Caelo	Hydroquinone	14281507	4

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Supplier	Substance	Batch	Spectra
Caelo	Hydroquinone	14281504	1
Caelo	Hydroquinone	16051502	1
Caelo	Hydroquinone	8816-10-583	1
Caelo	Hydroquinone	16023102	2
Caelo	Hydroquinone	16023105	12
Caelo	Hydroquinone	52840166	1
Caelo	Hydroquinone	160231135430	1
Caelo	Hydroquinone	16023116	16
Caelo	Hydroquinone	17221503	1
Caelo	Hydroquinone	20101806	1
Caelo	Hydroquinone	18017902	8
Caelo	Hydroquinone	8725	1
Caelo	Hydroquinone	16023113	7
Caelo	Hydroquinone	14180406	3
Caelo	Hydroquinone	10145113	2
Caelo	Hydroquinone	18230602	6
Caelo	Hydroquinone	14280105	2
Caelo	Hydroquinone	18230607	2
Caelo	Hydroquinone	3281	1
Caelo	Hydroquinone	10145101	1
Caelo	Hydroquinone	15057010	13
Caelo	Hydroquinone	15057002	1
Caelo	Hydroquinone	15023105	1
Caelo	Hydroquinone	4017A-01717	1
Caelo	Hydroquinone	1228503	1
Caelo	Hydroquinone	12288502	2
Caelo	Hydroquinone	13105405	6
Caelo	Hydroquinone	13105408	7
Caelo	Hydroquinone	17221508	4
Caelo	Hydroquinone	11163912	4
Caelo	Hydroquinone	16023118	12
Caelo	Hydroquinone	14280104	5
Caelo	Hydroquinone	1410401	1
Caelo	Hydroquinone	160223105	1
Caelo	Hydroquinone	18017905	1
Caeolo	Hydroquinone	16023105	1
Caeolo/Gehe	Hydroquinone	16023116	1
Caesar & Loretz GmbH	Hydroquinone	13105405	1
Caesar & Loretz GmbH	Hydroquinone	16023105	1
Caesar & Loretz GmbH	Hydroquinone	18230602	2
Caesar & Loretz GmbH, 4...	Hydroquinone	11163912	1
E Plus	Hydroquinone	18017902	1
Euro/Sanacorp	Hydroquinone	15057004	1
Fiebig	Hydroquinone	16023116	1
Gatt-Koller	Hydroquinone	1803302	4
Gehe	Hydroquinone	12156706	2
GEHE	Hydroquinone	16023105	1
GEHE	Hydroquinone	18017902	1
GEHE	Hydroquinone	16023118	1
Gehe/Gehe	Hydroquinone	14280110	1
Kehr	Hydroquinone	16023112	1
Kehr	Hydroquinone	16023113	1
Phoenix	Hydroquinone	16023105	1
Phoenix	Hydroquinone	18017905	1
Phoenix	Hydroquinone	18230602	1
Phoenix Goettin	Hydroquinone	14281501	1
phönix	Hydroquinone	16023105	1
Phönix	Hydroquinone	12288503	2
Phönix	Hydroquinone	13105408	1
Sanacorp	Hydroquinone	12288503	1

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Supplier	Substance	Batch	Spectra
Sanacorp	Hydroquinone	12156703	1
Sanacorp	Hydroquinone	16023103	1
Caelo	Hydroquinone		2
Caelo	Hydroquinone	15057004	12
Caelo	Hydroquinone	12288505	11
Caelo	Hydroquinone	14281501	10
Caelo	Hydroquinone	15057001	8
Caelo	Hydroquinone	14026904	1
Fagron	Hydroquinone		1

- 110 970 spectra from 742 *Apo-Ident* customers from a total of 31 824 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hydroquinone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hydroquinone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	480	0	110 209
Type B	0	80	0	119 062
Type C	0	273	4	110 970

The substance/substance group *Hydroquinone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	98.5560 % (> 97.4729 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hydroquinone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Resocrinol	14.52	—
Sodium cromoglicate	32.63	—
Levothyroxin sodium	42.07	—
Oxytetracycline hydrochloride	52.11	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hydroquinone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20884	21791	2.51	22.60
21468	21791	5.25	22.09
21791	21791	0.00	21.68
21923	21791	3.44	22.93
21975	21791	0.91	21.71
22324	21791	1.22	21.56
24761	24761	0.00	20.59
22351	21791	2.19	21.09
24890	24890	0.00	20.57

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s)
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20791-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s); Hydroxyethylcellulose (apparent viscosity 300 mPas); Hydroxyethylcellulose (apparent viscosity 5000 mPas); Hydroxyethylcellulose (apparent viscosity 9000 mPas); Hydroxyethylcellulose (nominal viscosity 300 mPas); Hydroxyethylcellulose (nominal viscosity 5000 mPas); Hydroxyethylcellulose (nominal viscosity 9000 mPas); Hydroxyethylcellulosum 250 M; Hydroxyethylcellulosum G 300; Hydroxyethylcellulosum HX

Special notes

When selecting the *Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydroxyethylcellulose (apparent viscosity 300 mPas)	9	6	270
Hydroxyethylcellulose (apparent viscosity 5000 mPas)	2	1	2
Hydroxyethylcellulose (apparent viscosity 9000 mPas)	3	2	52

Second-stage model

For differentiation of the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s) the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s):

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydroxyethylcell...	12249204	20791	40	20120830
Caelo	Hydroxyethylcell...	13378506	21365	40	1507205
Caelo	Hydroxyethylcell...	161006	22459	60	20160426*
Caelo	Hydroxyethylcell...	16278705	23710	40	20161014
Caelo	Hydroxyethylcell...	16278705	23759	40	20161014
Euro OTC	Hydroxyethylcell...	1110024-04	20792	40	20120110
Euro OTC	Hydroxyethylcell...	1804003	24060	40	20180413*
Euro OTC	Hydroxyethylcell...	1911004	24926	40	20191122*
Fagron	Hydroxyethylcell...	13H22-N11	20908	40	20130826
Fagron	Hydroxyethylcell...	16E09-B05-327042	23102	40	20160530
Caelo	Hydroxyethylcell...	171151	23349	40	20170523*
Caelo	Hydroxyethylcell...	190769	24502	40	20190425*
Caelo	Hydroxyethylcell...	03936475	20862	20	20121001
Caelo	Hydroxyethylcell...	14352504	21792	60	AR-15-FG-009318-01
Caelo	Hydroxyethylcell...	16252008	23708	40	20160907

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 620 spectra of 15 reference samples from the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s). These samples are listed above in the [calibration samples](#) section. The reference samples come from 14 different batches.
- 110 069 spectra from a total of 1952 batches from further 388 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A*

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s).
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydroxyethylcellulose (appar...	173196	23850	40
Caelo	Hydroxyethylcellulose (appar...	190767	24522	40
Euro OTC	Hydroxyethylcellulose (appar...	1606030	22698	40
Euro OTC	Hydroxyethylcellulose (appar...	1610039	22870	40
Euro OTC	Hydroxyethylcellulose (appar...	1711012	23904	40
Euro OTC	Hydroxyethylcellulose (appar...	1907013	24800	40
Caelo	Hydroxyethylcellulose (appar...	17115103	23863	40
Caelo	Hydroxyethylcellulose (appar...	16012909	22809	40
Caelo	Hydroxyethylcellulose (appar...	16252003	23584	40

- 118 782 spectra from a total of 2411 batches from further 797 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1374 spectra from 491 *Apo-Ident* customers from 324 batches from the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s).
- Among them are spectra of independent samples from 309 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Hydroxyethylcellulose (appar...	13153511	1
AHD	Hydroxyethylcellulose (appar...	15B04-B03-312859	1
Caelo	Hydroxyethylcellulose (appar...	1304008-01	1
Alliance Health 27.12.2...	Hydroxyethylcellulose (appar...	1304008-02	1
Alliance Healthcare	Hydroxyethylcellulose (appar...	16L07-B04-331846	1

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Supplier	Substance	Batch	Spectra
Alliance Healthcare/Hed...	Hydroxyethylcellulose (appar...	1309020-02	1
Anzag	Hydroxyethylcellulose (appar...	1110024-03	3
Anzag	Hydroxyethylcellulose (appar...	12249204	1
Anzag	Hydroxyethylcellulose (appar...	1606030-02	1
apo ident	Hydroxyethylcellulose (appar...	1606030-02	1
apo-ident	Hydroxyethylcellulose (appar...	N1535	1
apo-ident.	Hydroxyethylcellulose (appar...	1606030-02	1
Ashland	Hydroxyethylcellulose (appar...	130400801	1
Ashland Ind/Gehe	Hydroxyethylcellulose (appar...	140017-01	1
Ashland Industrie	Hydroxyethylcellulose (appar...	P515	1
Ashland Industries	Hydroxyethylcellulose (appar...	1711012-01	1
Ashland Industries/ All...	Hydroxyethylcellulose (appar...	1711012-01	1
Ashland Industries/Anzag	Hydroxyethylcellulose (appar...	L1891	1
Ashland/Sanacorp	Hydroxyethylcellulose (appar...	1309020-01	1
asland industries	Hydroxyethylcellulose (appar...	1711012-01	1
Bombastus	Hydroxyethylcellulose (appar...	1610039-02	1
Bombastus	Hydroxyethylcellulose (appar...	1606030-02	1
Caelo	Hydroxyethylcellulose (appar...	13153505	10
Caelo	Hydroxyethylcellulose (appar...	12548	1
Caelo	Hydroxyethylcellulose (appar...	12156902	1
Caelo	Hydroxyethylcellulose (appar...	12156901	1
Caelo	Hydroxyethylcellulose (appar...	1110024-02	2
Caelo	Hydroxyethylcellulose (appar...	12156908	4
Caelo	Hydroxyethylcellulose (appar...	5012I-03301	1
Caelo	Hydroxyethylcellulose (appar...	213I-03301	1
Caelo	Hydroxyethylcellulose (appar...	19011302	1
Caelo	Hydroxyethylcellulose (appar...	11186221	1
Caelo	Hydroxyethylcellulose (appar...	1113E-03301	1
Caelo	Hydroxyethylcellulose (appar...	20031305	1
Caelo	Hydroxyethylcellulose (appar...	10019408	2
Caelo	Hydroxyethylcellulose (appar...	8051305	1
Caelo	Hydroxyethylcellulose (appar...	122492014	1
Caelo	Hydroxyethylcellulose (appar...	12249216	5
Caelo	Hydroxyethylcellulose (appar...	12369713	2
Caelo	Hydroxyethylcellulose (appar...	13153501	8
Caelo	Hydroxyethylcellulose (appar...	25071301	1
Caelo	Hydroxyethylcellulose (appar...	26071301	1
Caelo	Hydroxyethylcellulose (appar...	13153502	1
Caelo	Hydroxyethylcellulose (appar...	13153506	7
Caelo	Hydroxyethylcellulose (appar...	12369718	1
Caelo	Hydroxyethylcellulose (appar...	10019402	2
Caelo	Hydroxyethylcellulose (appar...	13153511	7
Caelo	Hydroxyethylcellulose (appar...	1315306	1
Caelo	Hydroxyethylcellulose (appar...	31031402	1
Caelo	Hydroxyethylcellulose (appar...	13378508	3
Caelo	Hydroxyethylcellulose (appar...	19051406	1
Caelo	Hydroxyethylcellulose (appar...	13378507	9
Caelo	Hydroxyethylcellulose (appar...	130902001	1
Caelo	Hydroxyethylcellulose (appar...	10019406	2
Caelo	Hydroxyethylcellulose (appar...	220914PML02	1
Caelo	Hydroxyethylcellulose (appar...	1337807	1
Caelo	Hydroxyethylcellulose (appar...	21011502	1
Caelo	Hydroxyethylcellulose (appar...	1309020	1
Caelo	Hydroxyethylcellulose (appar...	13041502	1
Caelo	Hydroxyethylcellulose (appar...	13378516	2
Caelo	Hydroxyethylcellulose (appar...	15086403	3
Caelo	Hydroxyethylcellulose (appar...	16100612	4
Caelo	Hydroxyethylcellulose (appar...	15086407	7
Caelo	Hydroxyethylcellulose (appar...	15086503	1
Caelo	Hydroxyethylcellulose (appar...	140601702	1

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Supplier	Substance	Batch	Spectra
Caelo	Hydroxyethylcellulose (appar...	1504018-03	1
Caelo	Hydroxyethylcellulose (appar...	16100605	4
Caelo	Hydroxyethylcellulose (appar...	16100613	2
Caelo	Hydroxyethylcellulose (appar...	16100604	2
Caelo	Hydroxyethylcellulose (appar...	16100617	12
Caelo	Hydroxyethylcellulose (appar...	1606030-02	5
Caelo	Hydroxyethylcellulose (appar...	16100625	14
Caelo	Hydroxyethylcellulose (appar...	19041708	1
Caelo	Hydroxyethylcellulose (appar...	16278702	2
Caelo	Hydroxyethylcellulose (appar...	19081705	1
Caelo	Hydroxyethylcellulose (appar...	1606030-03	2
Caelo	Hydroxyethylcellulose (appar...	27101701	1
Caelo	Hydroxyethylcellulose (appar...	16278715	2
Caelo	Hydroxyethylcellulose (appar...	11121707	1
Caelo	Hydroxyethylcellulose (appar...	171101201	2
Caelo	Hydroxyethylcellulose (appar...	16278704	1
Caelo	Hydroxyethylcellulose (appar...	12031803	1
Caelo	Hydroxyethylcellulose (appar...	23041804	1
Caelo	Hydroxyethylcellulose (appar...	1610039-03	1
Caelo	Hydroxyethylcellulose (appar...	23061809	1
Caelo	Hydroxyethylcellulose (appar...	21071802	1
Caelo	Hydroxyethylcellulose (appar...	12091819	1
Caelo	Hydroxyethylcellulose (appar...	21111812	1
Caelo	Hydroxyethylcellulose (appar...	17319606	3
Caelo	Hydroxyethylcellulose (appar...	18113101	5
Caelo	Hydroxyethylcellulose (appar...	12011903	1
Caelo	Hydroxyethylcellulose (appar...	1731960608	1
Caelo	Hydroxyethylcellulose (appar...	173119613	1
Caelo	Hydroxyethylcellulose (appar...	17319625	4
Caelo	Hydroxyethylcellulose (appar...	19076703	2
Caelo	Hydroxyethylcellulose (appar...	16L07-B04-331244	1
Caelo	Hydroxyethylcellulose (appar...	17319615	1
Caelo	Hydroxyethylcellulose (appar...	1406017-01	4
Caelo	Hydroxyethylcellulose (appar...	16100626	7
Caelo	Hydroxyethylcellulose (appar...	N1535	1
Caelo	Hydroxyethylcellulose (appar...	17319603	3
Caelo	Hydroxyethylcellulose (appar...	18113107	1
Caelo	Hydroxyethylcellulose (appar...	11266305	1
Caelo	Hydroxyethylcellulose (appar...	12249202	3
Caelo	Hydroxyethylcellulose (appar...	14256002	2
Caelo	Hydroxyethylcellulose (appar...	AKD10	1
Caelo	Hydroxyethylcellulose (appar...	1610039-01	7
Caelo	Hydroxyethylcellulose (appar...	13378510	2
Caelo	Hydroxyethylcellulose (appar...	16100620	3
Caelo	Hydroxyethylcellulose (appar...	1610039-02	3
Caelo	Hydroxyethylcellulose (appar...	8639291	1
Caelo	Hydroxyethylcellulose (appar...	18C05-B05-354803	1
Caelo	Hydroxyethylcellulose (appar...	13378524	1
Caelo	Hydroxyethylcellulose (appar...	18C05-B05	1
Caelo	Hydroxyethylcellulose (appar...	12369704	9
Caelo	Hydroxyethylcellulose (appar...	1309020-01	2
Caelo	Hydroxyethylcellulose (appar...	16100603	1
Caelo	Hydroxyethylcellulose (appar...	17319613	6
Caelo	Hydroxyethylcellulose (appar...	17319620	1
Caelo	Hydroxyethylcellulose (appar...	11266316	1
Caelo	Hydroxyethylcellulose (appar...	13378515	3
Caelo	Hydroxyethylcellulose (appar...	4512I-03301	1
Caelo	Hydroxyethylcellulose (appar...	12369711	4
Caelo	Hydroxyethylcellulose (appar...	12369717	1
Caelo	Hydroxyethylcellulose (appar...	13378502	4

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Supplier	Substance	Batch	Spectra
Caelo	Hydroxyethylcellulose (appar...	140317	1
Caelo	Hydroxyethylcellulose (appar...	213M-03301	1
Caelo	Hydroxyethylcellulose (appar...	1337808	1
Caelo	Hydroxyethylcellulose (appar...	13378518	3
Caelo	Hydroxyethylcellulose (appar...	1504018-1	1
Caelo	Hydroxyethylcellulose (appar...	16100606	16
Caelo	Hydroxyethylcellulose (appar...	16100610	5
Caelo	Hydroxyethylcellulose (appar...	161003901	1
Caelo	Hydroxyethylcellulose (appar...	17J05-B03-342018	1
Caelo	Hydroxyethylcellulose (appar...	17319626	4
Caelo	Hydroxyethylcellulose (appar...	16012909	6
Caelo	Hydroxyethylcellulose (appar...	1804003-01	1
Caelo	Hydroxyethylcellulose (appar...	16278718	3
Caelo	Hydroxyethylcellulose (appar...	17319609	3
Caelo	Hydroxyethylcellulose (appar...	1304008-02	2
Caelo	Hydroxyethylcellulose (appar...	16100390108639291	1
Caelo	Hydroxyethylcellulose (appar...	12274720	1
Caelo	Hydroxyethylcellulose (appar...	133785	1
Caelo	Hydroxyethylcellulose (appar...	16100622	5
Caelo	Hydroxyethylcellulose (appar...	700243-B04-331244	1
Caelo	Hydroxyethylcellulose (appar...	17G05-B04-341204	2
Caelo	Hydroxyethylcellulose (appar...	16278714	7
Caelo	Hydroxyethylcellulose (appar...	17319602	4
Caelo	Hydroxyethylcellulose (appar...	19076708	6
Caelo	Hydroxyethylcellulose (appar...	19076704	1
Caelo	Hydroxyethylcellulose (appar...	1110024-04	1
Caelo	Hydroxyethylcellulose (appar...	15086505	1
Caelo	Hydroxyethylcellulose (appar...	15086408	1
Caelo	Hydroxyethylcellulose (appar...	15086504	2
Caelo	Hydroxyethylcellulose (appar...	16100607	1
Caelo	Hydroxyethylcellulose (appar...	18C05-B05-350300	1
Caelo	Hydroxyethylcellulose (appar...	17319621	1
Caelo	Hydroxyethylcellulose (appar...	1406017-02	4
Caelo	Hydroxyethylcellulose (appar...	15086405	7
Caelo	Hydroxyethylcellulose (appar...	140601701	1
Caelo	Hydroxyethylcellulose (appar...	15086507	1
Caelo	Hydroxyethylcellulose (appar...	16100615	5
Caelo	Hydroxyethylcellulose (appar...	16278708	1
Caelo	Hydroxyethylcellulose (appar...	16278719	1
Caelo	Hydroxyethylcellulose (appar...	160603001	2
Caelo	Hydroxyethylcellulose (appar...	1711012-01	4
Caelo	Hydroxyethylcellulose (appar...	17J05-B03	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	13153501	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319613	3
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	16278708	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319607	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319621	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319625	2
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319628	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	17319626	1
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	19076708	1
Caesar & Loretz GmbH, G...	Hydroxyethylcellulose (appar...	17319613	1
Caesar & Loretz GmbH/Kr...	Hydroxyethylcellulose (appar...	19076705	1
Caesar/Noweda	Hydroxyethylcellulose (appar...	13378507	1
Castor/Phönix	Hydroxyethylcellulose (appar...	1504018-01	1
Cealo	Hydroxyethylcellulose (appar...	1610039-01	2
Defektur	Hydroxyethylcellulose (appar...	1309020-01	1
Ebert & Jacobi 02.08.2016	Hydroxyethylcellulose (appar...	16100606	1
Caelo	Hydroxyethylcellulose (appar...	17319608	3
EuRho	Hydroxyethylcellulose (appar...	1110024-03	1

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Supplier	Substance	Batch	Spectra
EuRho	Hydroxyethylcellulose (appar...	1110024-04	1
EuRho	Hydroxyethylcellulose (appar...	3081202	1
EuRho	Hydroxyethylcellulose (appar...	1610039-03	1
EuRho AHC	Hydroxyethylcellulose (appar...	1610039-01	1
EuRho Phoenix	Hydroxyethylcellulose (appar...	160603001	1
EuRho Phoenix	Hydroxyethylcellulose (appar...	1711012-01	5
EuRho/ Noweda 5/19	Hydroxyethylcellulose (appar...	1711012-01	1
EuRho/GEHE	Hydroxyethylcellulose (appar...	1309020-03	1
EuRho/Phoenix	Hydroxyethylcellulose (appar...	1804003-01	1
EuRho/Phönix	Hydroxyethylcellulose (appar...	1711012-01	1
Euro OTC	Hydroxyethylcellulose (appar...	140601703	1
Euro OTC	Hydroxyethylcellulose (appar...	3081603	1
Euro OTC	Hydroxyethylcellulose (appar...	1406212528	1
Euro OTC	Hydroxyethylcellulose (appar...	1108027-01	1
Euro OTC	Hydroxyethylcellulose (appar...	1110024-03	17
Euro OTC	Hydroxyethylcellulose (appar...	K1371	2
Euro OTC	Hydroxyethylcellulose (appar...	130902001	1
Euro OTC	Hydroxyethylcellulose (appar...	12175708	1
Euro OTC	Hydroxyethylcellulose (appar...	1309020-03	11
Euro OTC	Hydroxyethylcellulose (appar...	1406017-01	36
Euro OTC	Hydroxyethylcellulose (appar...	1909020-02	1
Euro OTC	Hydroxyethylcellulose (appar...	1504018-01	18
Euro OTC	Hydroxyethylcellulose (appar...	1504019-02	1
Euro OTC	Hydroxyethylcellulose (appar...	1606030-01	40
Euro OTC	Hydroxyethylcellulose (appar...	16100603	1
Euro OTC	Hydroxyethylcellulose (appar...	161003901	3
Euro OTC	Hydroxyethylcellulose (appar...	1606030-03	4
Euro OTC	Hydroxyethylcellulose (appar...	160039-01	1
Euro OTC	Hydroxyethylcellulose (appar...	P0745	3
Euro OTC	Hydroxyethylcellulose (appar...	P1515	2
Euro OTC	Hydroxyethylcellulose (appar...	1804003-02	6
Euro OTC	Hydroxyethylcellulose (appar...	190701301	1
Euro OTC	Hydroxyethylcellulose (appar...	1309020-02	5
Euro OTC	Hydroxyethylcellulose (appar...	110505401	1
Euro OTC	Hydroxyethylcellulose (appar...	13040008-02	1
Euro OTC	Hydroxyethylcellulose (appar...	1500418-02	1
Euro OTC	Hydroxyethylcellulose (appar...	130400802	2
Euro OTC	Hydroxyethylcellulose (appar...	160603002	1
Euro OTC	Hydroxyethylcellulose (appar...	1110024-02	5
Euro OTC	Hydroxyethylcellulose (appar...	130400801	1
Euro OTC	Hydroxyethylcellulose (appar...	16603001	1
Euro OTC	Hydroxyethylcellulose (appar...	1110024-01	2
Euro OTC	Hydroxyethylcellulose (appar...	1304008-02	20
Euro OTC	Hydroxyethylcellulose (appar...	1309020-01	19
Euro OTC	Hydroxyethylcellulose (appar...	17042014A	1
Euro OTC	Hydroxyethylcellulose (appar...	13099020-01	1
Euro OTC	Hydroxyethylcellulose (appar...	13072015A	1
Euro OTC	Hydroxyethylcellulose (appar...	16060302-02	1
Euro OTC	Hydroxyethylcellulose (appar...	1804003-01	14
Euro OTC	Hydroxyethylcellulose (appar...	1304008-01	24
Euro OTC	Hydroxyethylcellulose (appar...	1406017	1
Euro OTC	Hydroxyethylcellulose (appar...	111024-02	1
Euro OTC	Hydroxyethylcellulose (appar...	80616-3	1
Euro OTC	Hydroxyethylcellulose (appar...	1108026-01	2
Euro OTC	Hydroxyethylcellulose (appar...	1105054-01	1
Euro OTC	Hydroxyethylcellulose (appar...	1406017-03	2
Euro OTC	Hydroxyethylcellulose (appar...	160603	1
Euro OTC	Hydroxyethylcellulose (appar...	41(1907013-01)	1
Euro OTC	Hydroxyethylcellulose (appar...	171101201	6
Euro OTC	Hydroxyethylcellulose (appar...	40(1711012-01)	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Hydroxyethylcellulose (appar...	180201HC/1610039-01	1
Euro OTC	Hydroxyethylcellulose (appar...	N1535	2
Euro OTC	Hydroxyethylcellulose (appar...	17319626	1
Euro OTC	Hydroxyethylcellulose (appar...	1610039-01	48
Euro OTC	Hydroxyethylcellulose (appar...	130902003	1
Euro OTC	Hydroxyethylcellulose (appar...	1610039-02	11
Euro OTC	Hydroxyethylcellulose (appar...	181102185	1
Euro OTC	Hydroxyethylcellulose (appar...	1711012	1
Euro OTC	Hydroxyethylcellulose (appar...	160603042	1
Euro OTC	Hydroxyethylcellulose (appar...	1907013-01	2
Euro/Sanacorp	Hydroxyethylcellulose (appar...	1610039-01	4
Euroo/Phoenix	Hydroxyethylcellulose (appar...	1304008-01	1
Euro OTC	Hydroxyethylcellulose (appar...	1406017-02	37
Euro OTC	Hydroxyethylcellulose (appar...	1504018-03	24
Euro OTC	Hydroxyethylcellulose (appar...	154018-02	1
Euro OTC	Hydroxyethylcellulose (appar...	1007018-01	1
Euro OTC	Hydroxyethylcellulose (appar...	161003903	1
Euro OTC	Hydroxyethylcellulose (appar...	1610039-03	9
Euro OTC	Hydroxyethylcellulose (appar...	1613M-03301	1
Euro OTC	Hydroxyethylcellulose (appar...	914E-03301	1
Euro OTC	Hydroxyethylcellulose (appar...	1504018-02	28
Euro OTC	Hydroxyethylcellulose (appar...	180400-03	1
Euro OTC	Hydroxyethylcellulose (appar...	1606030-02	25
Euro OTC	Hydroxyethylcellulose (appar...	1911004-01	1
Euro OTC	Hydroxyethylcellulose (appar...	140601702	1
Euro OTC	Hydroxyethylcellulose (appar...	161003902	2
Euro OTC	Hydroxyethylcellulose (appar...	160603001	2
Europharm/Otto	Hydroxyethylcellulose (appar...	1110024-03	1
Europharm/Otto	Hydroxyethylcellulose (appar...	1110024-04	2
Eurp	Hydroxyethylcellulose (appar...	130400801	2
Fagron	Hydroxyethylcellulose (appar...	15E07-B05-316511	3
Fagron	Hydroxyethylcellulose (appar...	11I02-N02	2
Fagron	Hydroxyethylcellulose (appar...	11I02-N12	1
Fagron	Hydroxyethylcellulose (appar...	12H02-N06	2
Fagron	Hydroxyethylcellulose (appar...	13L04-B03-289115	1
Fagron	Hydroxyethylcellulose (appar...	13L04-B03	1
Fagron	Hydroxyethylcellulose (appar...	14f04-b06-295130	1
Fagron	Hydroxyethylcellulose (appar...	14D04B02293555	1
Fagron	Hydroxyethylcellulose (appar...	14I04-B05	1
Fagron	Hydroxyethylcellulose (appar...	14I04-B05-300224	2
Fagron	Hydroxyethylcellulose (appar...	14I04-B05-300231	2
Fagron	Hydroxyethylcellulose (appar...	1404-B05-300231	1
Fagron	Hydroxyethylcellulose (appar...	14i04-b05-309049	1
Fagron	Hydroxyethylcellulose (appar...	15B04-B03-312859	3
Fagron	Hydroxyethylcellulose (appar...	14F04-B06-297846	1
Fagron	Hydroxyethylcellulose (appar...	15H28-B10	2
Fagron	Hydroxyethylcellulose (appar...	15H28-B10-319028	2
Fagron	Hydroxyethylcellulose (appar...	15b04-b03	1
Fagron	Hydroxyethylcellulose (appar...	17J05-B03-342018	3
Fagron	Hydroxyethylcellulose (appar...	17j05-b03-343927	1
Fagron	Hydroxyethylcellulose (appar...	17J05-B03-343927	3
Fagron	Hydroxyethylcellulose (appar...	17J05-B03-347890	9
Fagron	Hydroxyethylcellulose (appar...	18C05-B05-354803	4
Fagron	Hydroxyethylcellulose (appar...	17J05-B03	1
Fagron	Hydroxyethylcellulose (appar...	19C04-B08-191454	4
Fagron	Hydroxyethylcellulose (appar...	14F04-B06-295130	1
Fagron	Hydroxyethylcellulose (appar...	14I04-B05-309049	1
Fagron	Hydroxyethylcellulose (appar...	14D04-B02	2
Fagron	Hydroxyethylcellulose (appar...	18C05-B05-352498	4
Fagron	Hydroxyethylcellulose (appar...	12C27-N01	1

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Supplier	Substance	Batch	Spectra
Fagron	Hydroxyethylcellulose (appar...	12A09-N06	2
Fagron	Hydroxyethylcellulose (appar...	16107-b04-331244	1
Fagron	Hydroxyethylcellulose (appar...	16H05B05325803	1
Fagron	Hydroxyethylcellulose (appar...	K1373	2
Fagron	Hydroxyethylcellulose (appar...	14Io4-B05	1
Fagron	Hydroxyethylcellulose (appar...	16H05-B05-325803	2
Fagron	Hydroxyethylcellulose (appar...	14F04B06295130	1
Fagron	Hydroxyethylcellulose (appar...	14D04-B02-293558	2
Fagron	Hydroxyethylcellulose (appar...	16L07-B04-331846	2
Fagron	Hydroxyethylcellulose (appar...	15086403	1
Fagron	Hydroxyethylcellulose (appar...	18C05-B05-350300	1
Fagron	Hydroxyethylcellulose (appar...	1504018-02	1
Fagron	Hydroxyethylcellulose (appar...	14/04-B05-300231	1
Fagron	Hydroxyethylcellulose (appar...	16E09-B05-321320	4
Fagron	Hydroxyethylcellulose (appar...	16L07-B04-331244	6
Fagron	Hydroxyethylcellulose (appar...	17G05-B04-341204	14
Fagron	Hydroxyethylcellulose (appar...	17j05B03342018	1
Fagron	Hydroxyethylcellulose (appar...	1309020-01	1
Fagron	Hydroxyethylcellulose (appar...	1406017-02	2
Fagron	Hydroxyethylcellulose (appar...	15B04-B03-315495	1
Fagron	Hydroxyethylcellulose (appar...	16H05-B05	1
Fagron	Hydroxyethylcellulose (appar...	1711012-01	1
Fagron	Hydroxyethylcellulose (appar...	17G05-B04	3
Fagron	Hydroxyethylcellulose (appar...	13D26-N11	5
Fargon /Sanacorp	Hydroxyethylcellulose (appar...	19C04-B08-191454	1
fargon GmbH	Hydroxyethylcellulose (appar...	18C05-B05-352498	1
Fiebig	Hydroxyethylcellulose (appar...	1406017-02	1
Fiebig	Hydroxyethylcellulose (appar...	1406017-03	1
Fiebig	Hydroxyethylcellulose (appar...	1606030-02	1
Gatt-Koller	Hydroxyethylcellulose (appar...	1802575	1
Gehe	Hydroxyethylcellulose (appar...	12156908	1
Gehe	Hydroxyethylcellulose (appar...	13A18-N01	1
Gehe	Hydroxyethylcellulose (appar...	111002404	1
Gehe	Hydroxyethylcellulose (appar...	12369718	1
Gehe	Hydroxyethylcellulose (appar...	1406017-01	1
Gehe	Hydroxyethylcellulose (appar...	16100617	1
GEHE	Hydroxyethylcellulose (appar...	1610039-01	2
GEHE	Hydroxyethylcellulose (appar...	17319608	1
GEHE	Hydroxyethylcellulose (appar...	1711012-01	1
Caelo	Hydroxyethylcellulose (appar...	1504018-02	3
Gehe 24.06.2014	Hydroxyethylcellulose (appar...	13153505	1
Fagron	Hydroxyethylcellulose (appar...	13A18-N01	4
Caelo	Hydroxyethylcellulose (appar...	1606030-01	8
Caelo	Hydroxyethylcellulose (appar...	17Jo5-B03-343927	1
Euro OTC	Hydroxyethylcellulose (appar...	711012-01	1
gepepharm/Phönix	Hydroxyethylcellulose (appar...	160603002	1
hedinger	Hydroxyethylcellulose (appar...	1606030	1
Henry Lamotte/ Noweda	Hydroxyethylcellulose (appar...	1711012-01	1
Hepart	Hydroxyethylcellulose (appar...	1606030-01	1
Holdermann	Hydroxyethylcellulose (appar...	1110024-04	1
Kehr	Hydroxyethylcellulose (appar...	211112PML01	1
Kehr	Hydroxyethylcellulose (appar...	16278718	1
Caelo	Hydroxyethylcellulose (appar...	12249205	5
Caelo	Hydroxyethylcellulose (appar...	290114PML01	1
Kehr/ Ashland Industries	Hydroxyethylcellulose (appar...	1711012-01	2
L10	Hydroxyethylcellulose (appar...	1610039-01	1
L12	Hydroxyethylcellulose (appar...	16100626	1
L30	Hydroxyethylcellulose (appar...	1606030-03	1
Nachprüfung	Hydroxyethylcellulose (appar...	13d26-n16	1
Nachprüfung	Hydroxyethylcellulose (appar...	15086405	1

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Supplier	Substance	Batch	Spectra
Nachprüfung	Hydroxyethylcellulose (appar...	123456	1
Nachprüfung 2797	Hydroxyethylcellulose (appar...	12249202	1
Noweda	Hydroxyethylcellulose (appar...	1108027-01	1
Noweda	Hydroxyethylcellulose (appar...	13153501	1
Noweda	Hydroxyethylcellulose (appar...	13378507	1
Noweda	Hydroxyethylcellulose (appar...	13153511	1
Noweda	Hydroxyethylcellulose (appar...	1309020-03	1
Euro OTC	Hydroxyethylcellulose (appar...	1496017-02	1
Caelo	Hydroxyethylcellulose (appar...	15086506	1
Caelo	Hydroxyethylcellulose (appar...	16H05325803	1
Euro OTC	Hydroxyethylcellulose (appar...	150401801	1
Euro OTC	Hydroxyethylcellulose (appar...	1610036-01	1
Euro OTC	Hydroxyethylcellulose (appar...	1110024-04-336431909	1
Phoenix	Hydroxyethylcellulose (appar...	3115	1
Phoenix	Hydroxyethylcellulose (appar...	3236	1
Phoenix	Hydroxyethylcellulose (appar...	17319613	1
Phoenix 10.07.2014	Hydroxyethylcellulose (appar...	1309020-01	1
phoenix 23.11.18	Hydroxyethylcellulose (appar...	1711012-01	1
Phoenix Goettin	Hydroxyethylcellulose (appar...	14F04-B06-295130	1
Phonix	Hydroxyethylcellulose (appar...	1309020-01	1
phönix	Hydroxyethylcellulose (appar...	15e07b05316511	1
phönix	Hydroxyethylcellulose (appar...	1610039-02	1
Phönix	Hydroxyethylcellulose (appar...	12369711	1
Phönix	Hydroxyethylcellulose (appar...	12369704	1
Phönix	Hydroxyethylcellulose (appar...	13L04-B03-289115	2
Phönix	Hydroxyethylcellulose (appar...	1406017-02	1
Phönix	Hydroxyethylcellulose (appar...	16100606	1
Phönix WE:08.06.2015 ...	Hydroxyethylcellulose (appar...	1406017-02	2
Caelo	Hydroxyethylcellulose (appar...	18022401	4
Sanacorp	Hydroxyethylcellulose (appar...	12156901	1
Sanacorp	Hydroxyethylcellulose (appar...	1110024-03	1
Sanacorp	Hydroxyethylcellulose (appar...	12H02-N06	1
Sanacorp	Hydroxyethylcellulose (appar...	1606030-03	1
Sanacorp	Hydroxyethylcellulose (appar...	16278705	1
Euro OTC	Hydroxyethylcellulose (appar...	1711012-01	75
Fagron	Hydroxyethylcellulose (appar...	J0696	2
Caelo	Hydroxyethylcellulose (appar...	1110024-01	1
Fagron	Hydroxyethylcellulose (appar...	15086407	1
Sanacorp/Phoenix	Hydroxyethylcellulose (appar...	1309020-01	1
Spangro_17.01.2019	Hydroxyethylcellulose (appar...	17319603	1
Th. Geyer	Hydroxyethylcellulose (appar...	13L04-B03	1
Caelo	Hydroxyethylcellulose (appar...	12156907	9
Euro OTC	Hydroxyethylcellulose (appar...	1804003_01	1
Bombastus	Hydroxyethylcellulose (appar...	14095911	1
Caelo	Hydroxyethylcellulose (appar...	11304620	4
Caelo	Hydroxyethylcellulose (appar...	12274710	2
Caelo	Hydroxyethylcellulose (appar...	13182702	6
Caelo	Hydroxyethylcellulose (appar...	12274702	1
Caelo	Hydroxyethylcellulose (appar...	14352508	1
Caelo	Hydroxyethylcellulose (appar...	14352510	4
Caelo	Hydroxyethylcellulose (appar...	15199501	11
Caelo	Hydroxyethylcellulose (appar...	15199510	1
Caelo	Hydroxyethylcellulose (appar...	16012901	1
Caelo	Hydroxyethylcellulose (appar...	16252003	2
Caelo	Hydroxyethylcellulose (appar...	16252006	7
Caelo	Hydroxyethylcellulose (appar...	4091713	1
Caelo	Hydroxyethylcellulose (appar...	16091711	1
Caelo	Hydroxyethylcellulose (appar...	17184503	7
Caelo	Hydroxyethylcellulose (appar...	5121706	1
Caelo	Hydroxyethylcellulose (appar...	9041802	1

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Supplier	Substance	Batch	Spectra
Caelo	Hydroxyethylcellulose (appar...	9061802	1
Caelo	Hydroxyethylcellulose (appar...	18022503	1
Caelo	Hydroxyethylcellulose (appar...	17101801	1
Caelo	Hydroxyethylcellulose (appar...	18022507	2
Caelo	Hydroxyethylcellulose (appar...	28111805	1
Caelo	Hydroxyethylcellulose (appar...	23011901	1
Caelo	Hydroxyethylcellulose (appar...	28111804	1
Caelo	Hydroxyethylcellulose (appar...	19034901	1
Caelo	Hydroxyethylcellulose (appar...	19167502	1
Caelo	Hydroxyethylcellulose (appar...	14095911	3
Caelo	Hydroxyethylcellulose (appar...	14095905	1
Caelo	Hydroxyethylcellulose (appar...	18022505	6
Caelo	Hydroxyethylcellulose (appar...	14095901	1
Caelo	Hydroxyethylcellulose (appar...	18113110	1
Caelo	Hydroxyethylcellulose (appar...	13182714	1
Caelo	Hydroxyethylcellulose (appar...	18022502	5
Caesar & Loretz GmbH	Hydroxyethylcellulose (appar...	18113101	1
Caesar & Loretz GmbH D-...	Hydroxyethylcellulose (appar...	12274702	1
Euro OTC	Hydroxyethylcellulose (appar...	146017-02	1
Euro OTC	Hydroxyethylcellulose (appar...	16012909	1
Euro OTC	Hydroxyethylcellulose (appar...	314Q3301	1
Euro OTC	Hydroxyethylcellulose (appar...	11110024-03	1
Fagron	Hydroxyethylcellulose (appar...	130902002	1
Fagron	Hydroxyethylcellulose (appar...	14352504	1
Fagron	Hydroxyethylcellulose (appar...	13d26-n16	1
Gehe	Hydroxyethylcellulose (appar...	18022502	1
Gehe	Hydroxyethylcellulose (appar...	18022505	1
Gutenberg-Apotheke	Hydroxyethylcellulose (appar...	11048105	1
Jenne	Hydroxyethylcellulose (appar...	15199501	1
L12	Hydroxyethylcellulose (appar...	18022505	1
L30	Hydroxyethylcellulose (appar...	17184503	1
Phönix	Hydroxyethylcellulose (appar...	1304008-02	1
PHÖNIX	Hydroxyethylcellulose (appar...	18022505	1
Rezepturlager - Verläng...	Hydroxyethylcellulose (appar...	54/16	1
	Hydroxyethylcellulose (appar...	1304008-01	1
Caelo	Hydroxyethylcellulose (appar...	12249204	2
Caelo	Hydroxyethylcellulose (appar...	13378506	3
Caelo	Hydroxyethylcellulose (appar...	16278705	14
Euro OTC	Hydroxyethylcellulose (appar...	1110024-04	17
Fagron	Hydroxyethylcellulose (appar...	13H22-N11	8
s.Prüfprotokoll	Hydroxyethylcellulose (appar...		2
Fagron	Hydroxyethylcellulose (appar...	16E09-B05-327042	1
Sanacorp/Ichthyol	Hydroxyethylcellulose (appar...		1
Caelo	Hydroxyethylcellulose (appar...	16252008	3
Euro OTC	Hydroxyethylcellulose (appar...	1804003	1

- 109873 spectra from 742 *Apo-Ident* customers from a total of 31 577 batches from a further 704 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s) can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with

Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s) and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (A/B/C).

	False positive	True positive	False negative	True negative
Type A	0	620	0	110 069
Type B	0	360	0	118 665
Type C	0	1369	5	109 873

The substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s) can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0323 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8899 %)	99.6361 % (> 99.4178 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s) in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium citrate tetrahydrate	53.01	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hydroxyethylcelluloses* (300 / 5000/ 9000 mPa · s) is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20862	22459	5.24	56.31
21792	21792	0.00	58.22
23708	21792	2.93	57.67

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20791	24926	7.88	55.40
20792	24060	8.92	54.14
20908	24060	11.85	53.01
21365	21365	0.00	56.37
22459	22459	0.00	57.21
23102	24060	4.41	56.54
23710	24060	7.10	55.70
23759	24060	8.52	55.76
24060	24060	0.00	56.18
24926	24926	0.00	57.81
23349	23349	0.00	60.84
24502	24502	0.00	59.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hyoscine butylbromide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20766-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hyoscine butylbromide; Hyoscini butylbromidum

Special notes

When selecting the *Hyoscine butylbromide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hyoscine butylbromide	4	2	1

Second-stage model

For differentiation of the substance/substance group *Hyoscine butylbromide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hyoscine butylbromide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Hyoscine butylbr...	12K01-N07	20766	40	1406057
Fagron	Hyoscine butylbr...	12K01-N07	20897	40	20121102
Fagron	Hyoscine butylbr...	13K22-N03	21049	40	20131126
Fagron	Hyoscine butylbr...	15I09-B04-312245	21954	60	20150921
Fagron	Hyoscine butylbr...	18A03-B01-352889	24576	40	20180122

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Hyoscine butylbromide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Hyoscine butylbromide*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Hyoscine butylbromide	15I09-B04-316806	22344	60
Fagron	Hyoscine butylbromide	16I20-B08-326942	22903	40
Fagron	Hyoscine butylbromide	16I20-B08-326942	22937	40

- 119 002 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 4 *Apo-Ident* customers from 1 batches from the substance/substance group *Hyoscine butylbromide*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Hyoscine butylbromide	16I20-B08-326942	12

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hyoscine butylbromide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hyoscine butylbromide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	140	0	119 002
Type C	0	12	0	111 235

The substance/substance group *Hyoscine butylbromide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hyoscine butylbromide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	50.56	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hyoscine butylbromide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20766	20766	0.00	89.15
20897	20766	12.78	84.56
21049	20766	5.59	87.35
21954	20766	6.00	87.79
24576	20766	6.75	88.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Hyoscine hydrobromide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21676-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Hyoscine hydrobromide; Scopolamini hydrobromidum

Special notes

When selecting the *Hyoscine hydrobromide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hyoscine hydrobromide	6	1	12

Second-stage model

For differentiation of the substance/substance group *Hyoscine hydrobromide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Hyoscine hydrobromide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hyoscine hydrobr...	14278801	21676	60	1504154
Caelo	Hyoscine hydrobr...	15054501	21764	60	1511156
Caelo	Hyoscine hydrobr...	15054501	21764SI	28	1511156
Caelo	Hyoscine hydrobr...	190869	24880	40	20190604*
Caelo	Hyoscine hydrobr...	190869	24880SI	40	20190604*
Caelo	Hyoscine hydrobr...	172303	24881	40	20170926*
Fagron	Hyoscine hydrobr...	15L09-B04-334706	23418	40	20151228
Fagron	Hyoscine hydrobr...	15L09-B04-334706	23418SI	40	20151228
Fagron	Hyoscine hydrobr...	15L09-B04-334706	23419	40	20151228
Fagron	Hyoscine hydrobr...	15L09-B04-334706	23419SI	40	20151228
Fagron	Hyoscine hydrobr...	19G29-B02-367045	25042	40	20191223

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 468 spectra of 11 reference samples from the substance/substance group *Hyoscine hydrobromide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 221 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 282 spectra of 7 reference samples from the substance/substance group *Hyoscine hydrobromide*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hyoscine hydrobromide	15054504	21925	60
Caelo	Hyoscine hydrobromide	15054501	21764SI [†]	32
Caelo	Hyoscine hydrobromide	15054504	21925SI	30
Caelo	Hyoscine hydrobromide	15054504	23441	40
Caelo	Hyoscine hydrobromide	15054504	23441SI	40
Caelo	Hyoscine hydrobromide	172303	24881SI [†]	40
Fagron	Hyoscine hydrobromide	19G29-B02-367045	25042SI [†]	40

- 118 860 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 41 spectra from 14 *Apo-Ident* customers from 13 batches from the substance/substance group *Hyoscine hydrobromide*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Hyoscine hydrobromide	15358901	1
Caelo	Hyoscine hydrobromide	15054505	1
Caelo	Hyoscine hydrobromide	16206208	1
Caelo	Hyoscine hydrobromide	17230303	1
Caelo	Hyoscine hydrobromide	18024807	1
Caelo	Hyoscine hydrobromide	16206204	1
Caelo	Hyoscine hydrobromide	18024806	4
Caelo	Hyoscine hydrobromide	15054511	1
Caelo	Hyoscine hydrobromide	19086901	1
Fagron	Hyoscine hydrobromide	14F11-B02-296840	1
Fagron	Hyoscine hydrobromide	18B23-B04-357420	1
Fagron	Hyoscine hydrobromide	14J27-B05-307020	1
Caelo	Hyoscine hydrobromide	14278801	26

- 111 206 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Hyoscine hydrobromide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Hyoscine hydrobromide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	468	0	110 221
Type B	0	275	7	118 860
Type C	0	41	0	111 206

The substance/substance group *Hyoscine hydrobromide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7179 %)
Type B	100.0000 % (> 99.9893 %)	97.5177 % (> 96.4539 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 85.3659 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Hyoscine hydrobromide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinine hydrochloride	39.78	—
Ephedrine hydrochloride	45.50	—
L-carnitine tartrate	51.09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Hyoscine hydrobromide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23418	21764	13.75	39.78
23419	21764	8.58	40.62
24880	24880	0.00	40.67
21676	21676	0.00	31.20
24881	24881	0.00	25.21
25042	21676	4.37	30.56
21764	21764	0.00	31.99

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ibuprofen**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20205-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ibuprofen; Ibuprofenum

Special notes

When selecting the *Ibuprofen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ibuprofen	4	2	9

Second-stage model

For differentiation of the substance/substance group *Ibuprofen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ibuprofen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ibuprofen	11352219	20774	40	20120124
Caelo	Ibuprofen	172271	23641	40	20170831*
Euro OTC	Ibuprofen	1211011-02	21248	40	1501533
Euro OTC	Ibuprofen	1410025-02	23587	40	20141125

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Ibuprofen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Ibuprofen*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ibuprofen	13105108	21321	40
Caelo	Ibuprofen	183003	24557	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 23 spectra from 13 *Apo-Ident* customers from 10 batches from the substance/substance group *Ibuprofen*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Ibuprofen	1410025-02	1
Caelo	Ibuprofen	17227101	1
Caelo	Ibuprofen	17227102	1
Caelo	Ibuprofen	18300304	1
Caelo	Ibuprofen	17351401	3
Euro OTC	Ibuprofen	9061807	1
Euro OTC	Ibuprofen	1410025-01	6
Euro OTC	Ibuprofen	1211011-01	1
GEHE	Ibuprofen	15103011	1
Caelo	Ibuprofen		1
Euro OTC	Ibuprofen	1410025-02	6

- 111 224 spectra from 742 *Apo-Ident* customers from a total of 31 881 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ibuprofen* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ibuprofen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	80	0	119 062
Type C	0	21	2	111 224

The substance/substance group *Ibuprofen* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	91.3043 % (> 78.2609 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ibuprofen* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methacholine chloride	41.00	—
Tetracaine base	41.91	—
Sildenafil citrate	46.63	—
Omeprazole	47.98	—
Metoprolol tartrate	56.04	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ibuprofen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20774	21248	6.63	49.10
21248	21248	0.00	45.86
23587	21248	5.33	46.12
23641	23641	0.00	42.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Indometacin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20720-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Indometacin; Indometacinum

Special notes

When selecting the *Indometacin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Indometacin	5	2	19

Second-stage model

For differentiation of the substance/substance group *Indometacin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Indometacin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Indometacin	1012009-02	20720	40	1402050
Euro OTC	Indometacin	1205002-01	21327	40	20120521
Euro OTC	Indometacin	1512031	22291	60	20160122*
Euro OTC	Indometacin	1612017	22981	40	20170209*
Fagron	Indometacin	18H14-B04-365453	25062	40	20180920

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Indometacin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Indometacin*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Indometacin	1801040	23969	40
Fagron	Indometacin	17I08-B06-339738	23715	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 69 spectra from 33 *Apo-Ident* customers from 21 batches from the substance/substance group *Indometacin*.
- Among them are spectra of independent samples from 19 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Indometacin	1801040-01	3
Caelo	Indometacin	1801040-02	1
Euro OTC	Indometacin	1801040-02	4
Euro OTC	Indometacin	1612017-01	6
Euro OTC	Indometacin	2091716	1
Euro OTC	Indometacin	1612017-2	1
Euro OTC	Indometacin	27101709	1
Euro OTC	Indometacin	16110102	1
Euro OTC	Indometacin	612017-02	1
Euro OTC	Indometacin	180104002	1
Euro OTC	Indometacin	201612162018	1
Euro OTC	Indometacin	1512031-01	14
Euro OTC	Indometacin	180104001	1
Euro OTC	Indometacin	201606272030	1
Euro OTC	Indometacin	1612017-02	7
Euro OTC	Indometacin	1801040-01	12
Fagron	Indometacin	17I08B06	1
Fagron	Indometacin	18H14-B03-352947	1
Fagron	Indometacin	17I08-B06-339738	2
Fagron	Indometacin	14I25-B02-303648	1
Fagron	Indometacin	14I08-B06-343286	1
Gehe	Indometacin	1512031-01	1
Noweda	Indometacin	1801040-01	3
Euro OTC	Indometacin	1205002-01	2
Fagron	Indometacin		1

- 111 178 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Indometacin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Indometacin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	68	1	111 178

The substance/substance group *Indometacin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	98.5507 % (> 94.2029 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Indometacin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	48.57	—
Thalidomide	70.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Indometacin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20720	20720	0.00	69.17
21327	22981	3.54	69.87
22291	22291	0.00	66.80
22981	22981	0.00	64.31
25062	22981	2.84	69.54

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Inositol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20420-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Inositol; Inositolium

Special notes

When selecting the *Inositol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Inositol	2	2	5

Second-stage model

For differentiation of the substance/substance group *Inositol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Inositol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Inositol	1206032-01	21280	40	20120814
Fagron	Inositol	13D15-B40-328250	23405	40	20140812
Fagron	Inositol	13D15-B40-328250	23406	40	AR-17-FG-016393-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Inositol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 569 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Inositol*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Inositol	L1507021-01	22797	40
Fagron	Inositol	18A03-B04-344527	23999	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the

substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 5 *Apo-Ident* customers from 5 batches from the substance/substance group *Inositol*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Cielo	Inositol	L1609025-01	1
Euro OTC	Inositol	130400901	1
Euro OTC	Inositol	1609025-01	1
Euro OTC	Inositol	1304009-01	1
Fagron	Inositol	L13090200	1

- 111 242 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Inositol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Inositol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	80	0	119 062
Type C	0	5	0	111 242

The substance/substance group *Inositol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Inositol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	28.90	—
Xylitol	36.65	—
Aciclovir	52.15	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Inositol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21280	23406	3.91	25.72
23405	23406	1.91	26.42
23406	23406	0.00	26.17

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Iodoform
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20094-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Iodoform; Iodoformium

Special notes

When selecting the *Iodoform* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Iodoform	4	3	109

Second-stage model

For differentiation of the substance/substance group *Iodoform* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Iodoform*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Iodoform	12283206	21297	40	20130709
Caelo	Iodoform	16012302	23192	40	AR-17-FG-012459-01
Caelo	Iodoform	16012302	23407	40	20160211
Caelo	Iodoform	191132	24710	40	20190524*
Fagron	Iodoform	12L11-B41	21278	40	20140113

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Iodoform*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 489 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 110 spectra of 3 reference samples from the substance/substance group *Iodoform*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Iodoform	170860	23652	30
Caelo	Iodoform	180919	24012	40
Caelo	Iodoform	182495	24380	40

- 119032 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 352 spectra from 154 *Apo-Ident* customers from 112 batches from the substance/substance group *Iodoform*.
- Among them are spectra of independent samples from 109 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Iodoform	14230001	6
Caelo	Iodoform	12150908	4
Caelo	Iodoform	3041407	1
Caelo	Iodoform	12070102	2
Caelo	Iodoform	12070303	2
Caelo	Iodoform	12150903	1
Caelo	Iodoform	12070606	2
Caelo	Iodoform	21051305	1
Caelo	Iodoform	12070407	1
Caelo	Iodoform	12070601	4
Caelo	Iodoform	12283201	3
Caelo	Iodoform	12283303	2
Caelo	Iodoform	12283304	1
Caelo	Iodoform	14077606	2
Caelo	Iodoform	14229507	3
Caelo	Iodoform	14229504	2
Caelo	Iodoform	14230002	3
Caelo	Iodoform	28011503	1
Caelo	Iodoform	14229505	1
Caelo	Iodoform	15276002	4
Caelo	Iodoform	15276104	4
Caelo	Iodoform	1576103	1
Caelo	Iodoform	15276108	2
Caelo	Iodoform	15276111	6
Caelo	Iodoform	1527104	1
Caelo	Iodoform	10320407	1
Caelo	Iodoform	16012205	2
Caelo	Iodoform	23021715	1
Caelo	Iodoform	16012202	2
Caelo	Iodoform	16012207	4
Caelo	Iodoform	16012210	6
Caelo	Iodoform	16012309	5
Caelo	Iodoform	12070105	1
Caelo	Iodoform	16012311	1
Caelo	Iodoform	17086005	9

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Supplier	Substance	Batch	Spectra
Caelo	Iodoform	17086001	1
Caelo	Iodoform	17086004	8
Caelo	Iodoform	18041821	1
Caelo	Iodoform	17086003	2
Caelo	Iodoform	18091905	9
Caelo	Iodoform	18091902	1
Caelo	Iodoform	18091807	1
Caelo	Iodoform	18091909	1
Caelo	Iodoform	17086008	3
Caelo	Iodoform	14230006	4
Caelo	Iodoform	16012201	7
Caelo	Iodoform	12283307	1
Caelo	Iodoform	18249502	2
Caelo	Iodoform	12150910	5
Caelo	Iodoform	14229508	2
Caelo	Iodoform	12070602	3
Caelo	Iodoform	12150907	1
Caelo	Iodoform	12150905	3
Caelo	Iodoform	14230304	2
Caelo	Iodoform	18091804	3
Caelo	Iodoform	46(18091805)	1
Caelo	Iodoform	47(18091905)	1
Caelo	Iodoform	49(18091911)	1
Caelo	Iodoform	18091801	1
Caelo	Iodoform	17086012	2
Caelo	Iodoform	14077702	7
Caelo	Iodoform	15276109	2
Caelo	Iodoform	16012206	6
Caelo	Iodoform	18091912	1
Caelo	Iodoform	19113201	1
Caelo	Iodoform	12070605	1
Caelo	Iodoform	12070608	3
Caelo	Iodoform	12283202	5
Caelo	Iodoform	14077603	2
Caelo	Iodoform	14077601	1
Caelo	Iodoform	14230305	7
Caelo	Iodoform	15276101	5
Caelo	Iodoform	1010316	1
Caelo	Iodoform	17086002	3
Caelo	Iodoform	48(18091905)	1
Caelo	Iodoform	14230007	3
Caelo	Iodoform	14230003	1
Caelo	Iodoform	14230008	3
Caelo	Iodoform	14230306	5
Caelo	Iodoform	1527611	1
Caelo	Iodoform	16012204	5
Caelo	Iodoform	12070502	1
Caelo	Iodoform	12150902	6
Caelo	Iodoform	15276103	5
Caelo	Iodoform	15276107	1
Caelo	Iodoform	16012305	5
Caelo	Iodoform	18091911	1
Caelo	Iodoform	14077602	1
Caelo	Iodoform	15276102	5
Caelo	Iodoform	15276105	7
Caelo	Iodoform	15276113	1
Caelo	Iodoform	18091806	6
Caelo	Iodoform	14077607	1
Caelo	Iodoform	14230308	6
Caelo	Iodoform	16012306	6

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Supplier	Substance	Batch	Spectra
Caelo	Iodoform	16012308	3
Caelo	Iodoform	18091802	5
Caelo	Iodoform	18091805	11
Caelo	Iodoform	18091906	1
Caelo	Iodoform	14230302	2
Caelo	Iodoform	15276001	3
Caesar & Loretz GmbH	Iodoform	12150907	1
Caesar & Loretz GmbH	Iodoform	18091905	1
Caesar & Loretz GmbH	Iodoform	18249502	2
Caesar & Loretz GmbH	Iodoform	19113201	1
Caesar & Loretz GmbH, 4...	Iodoform	12070501	3
Caesar u.Loretz	Iodoform	16012209	2
Euro OTC	Iodoform	14229504	2
Fagron	Iodoform	12E30-N01	2
Fagron	Iodoform	12L11-B41-290055	1
Fagron	Iodoform	14D09-B14-293029	1
Fagron	Iodoform	14229508	1
Fagron	Iodoform	16012302	1
Fagron	Iodoform	18091803	1
Fiebig	Iodoform	16012206	1
fragon	Iodoform	12283303	1
Gehe	Iodoform	14230008	1
GEHE	Iodoform	17086003	1
GEHE	Iodoform	17086002	1
Midas	Iodoform	16012306	1
Nachprüfung von Juni 2018	Iodoform	15276103	1
Noweda	Iodoform	10320402	1
Noweda	Iodoform	12070407	1
Noweda	Iodoform	18091806	1
Phoenix	Iodoform	12070601	1
phönix	Iodoform	18249502	2
Caelo	Iodoform	17086006	10
Sanacorp	Iodoform	17086005	1
Caelo	Iodoform	12070501	1
Caelo	Iodoform	16012302	5
Caelo	Iodoform	12283206	3
Fagron	Iodoform	12L11-B41	1

- 110 895 spectra from 742 *Apo-Ident* customers from a total of 31 780 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Iodoform* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Iodoform* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	110	0	119 032
Type C	0	345	7	110 895

The substance/substance group *Iodoform* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 94.5455 %)
Type C	100.0000 % (> 99.8899 %)	98.0114 % (> 97.1591 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Iodoform* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	86.63	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Iodoform* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24710	24710	0.00	93.65
21278	24710	7.73	95.42
21297	24710	9.47	97.66
23192	23192	0.00	92.06
23407	24710	5.43	94.11

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ipratropium bromide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20911-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ipratropium bromide; Ipratropii bromidum

Special notes

When selecting the *Ipratropium bromide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ipratropium bromide	3	3	2

Second-stage model

For differentiation of the substance/substance group *Ipratropium bromide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ipratropium bromide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ipratropium brom...	12C15-N01	20911	40	1403675
Fagron	Ipratropium brom...	12K01-N08	21272	40	20121025
Fagron	Ipratropium brom...	18H30-B09-359179	24947	40	20180918

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Ipratropium bromide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Ipratropium bromide*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ipratropium bromide	15C04-B02-321674	22747	40
Fagron	Ipratropium bromide	16K07-B05-335330	23597	40
Fagron	Ipratropium bromide	18B19-B05-346997	23992	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Ipratropium bromide*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Ipratropium bromide	18B19-B05-348556	1
Fagron	Ipratropium bromide	14B05-B16-294566	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ipratropium bromide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ipratropium bromide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	119	1	119 022
Type C	0	2	0	111 245

The substance/substance group *Ipratropium bromide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	99.1667 % (> 96.6667 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ipratropium bromide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fluocinoloneacetonid, micronized	44.81	—
Procaine hydrochloride	51.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ipratropium bromide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24947	20911	9.60	59.70
20911	20911	0.00	58.02
21272	20911	1.49	56.61

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Isoleucine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21045-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Isoleucine; Isoleucinum; L-isoleucine

Special notes

When selecting the *Isoleucine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Isoleucine	5	7	11

Second-stage model

For differentiation of the substance/substance group *Isoleucine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Isoleucine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Isoleucine	1604057	22566	40	20160601*
Euro OTC	Isoleucine	1704022	23386	40	20170612*
Euro OTC	Isoleucine	1909025	24931	40	20191015*
Fagron	Isoleucine	13E02-B01-286930	21045	40	1403154
Fagron	Isoleucine	13E02-B01	21332	40	20130621

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Isoleucine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 489 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 8 reference samples from the substance/substance group *Isoleucine*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Isoleucine	L1211010-02	21535	60
Euro OTC	Isoleucine	1611007	22869	40
Euro OTC	Isoleucine	1708027	23702	40
Euro OTC	Isoleucine	1711034	23869	40
Euro OTC	Isoleucine	1803019	24080	40
Euro OTC	Isoleucine	1805013	24115	40
Euro OTC	Isoleucine	1901010	24515	40
Euro OTC	Isoleucine	L1211010-02	21581	60

- 118 782 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 15 spectra from 9 *Apo-Ident* customers from 12 batches from the substance/substance group *Isoleucine*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Isoleucine	1704022-01	1
Euro OTC	Isoleucine	1708027-01	1
Euro OTC	Isoleucine	1711034-01	1
Euro OTC	Isoleucine	1901010-01	1
Fagro WE:19.05.16 EK:64...	Isoleucine	15A14-B09-314881	1
Fagron	Isoleucine	13A22-N03	1
Fagron	Isoleucine	12080167	1
Fagron	Isoleucine	16H24-B03-331739	1
Fagron	Isoleucine	17H14-B04-339008	2
Sanacorp	Isoleucine	17H14-B04-339008	1
Fagron	Isoleucine	14D08-B02-296089	2
Synop WE:18.12.17 E.K:...	Isoleucine	17H14-B04-339009	1
Fagron	Isoleucine	13E02-B01-286930	1

- 111 232 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Isoleucine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isoleucine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	359	1	118 782
Type C	0	15	0	111 232

The substance/substance group *Isoleucine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	99.7222 % (> 98.8889 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Isoleucine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-leucine	27.99	—
Levocarnitine	35.76	—
Xylometazoline hydrochloride	47.52	—
Valine	49.39	—
Mometasone furoate, micronized	62.29	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Isoleucine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21045	21045	0.00	41.50
21332	22566	4.07	40.38
22566	22566	0.00	35.95
23386	23386	0.00	37.41
24931	24931	0.00	32.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Isosorbide dinitrate 40%**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20213-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Isosorbide dinitrate 40%; Isorbidi dinitras 40%

Special notes

When selecting the *Isosorbide dinitrate 40%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Isosorbide dinitrate 40%	4	2	141

Second-stage model

For differentiation of the substance/substance group *Isosorbide dinitrate 40%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Isosorbide dinitrate 40%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Isosorbide dinit...	12F08-N04	20891	40	20120801
Fagron	Isosorbide dinit...	13D15-N02	21347	39	20130410
Fagron	Isosorbide dinit...	15I10-B01-328577	23200	40	1709092
Fagron	Isosorbide dinit...	15I10-B01-328577	23598	30	20150922
Fagron	Isosorbide dinit...	17C29-B01-339447	24057	40	20170517

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 189 spectra of 5 reference samples from the substance/substance group *Isosorbide dinitrate 40%*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 500 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Isosorbide dinitrate 40%*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Isosorbide dinitrate 40%	15I10-B01-315217	22762	40
Fagron	Isosorbide dinitrate 40%	18J18-B01-363845	25065	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 455 spectra from 198 *Apo-Ident* customers from 162 batches from the substance/substance group *Isosorbide dinitrate 40%*.
- Among them are spectra of independent samples from 141 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Isosorbide dinitrate 40%	17C29B01348859	1
Fagron	Isosorbide dinitrate 40%	15I10-B01-331286	2
AHD	Isosorbide dinitrate 40%	17C29-B01-350470	1
AHD 09.03.2015	Isosorbide dinitrate 40%	14D09-B03-294281	1
Allianz Healthcare 17.0...	Isosorbide dinitrate 40%	14D09-B03-300234	1
Anzag	Isosorbide dinitrate 40%	12C08-N05	2
Anzag	Isosorbide dinitrate 40%	1510B01315217	1
Anzag	Isosorbide dinitrate 40%	15/10-B01-328577	1
Fagron	Isosorbide dinitrate 40%	13A07-N13	7
Caelo	Isosorbide dinitrate 40%	15I10-B01-325474	1
Caelo	Isosorbide dinitrate 40%	13D15-N02	3
Caelo	Isosorbide dinitrate 40%	13/26-N18	1
Caelo	Isosorbide dinitrate 40%	14D09B03294281	1
Caelo	Isosorbide dinitrate 40%	13F27-N04	1
Caelo	Isosorbide dinitrate 40%	14D09-B03-307018	1
Caelo	Isosorbide dinitrate 40%	1510b1320782	1
Caelo	Isosorbide dinitrate 40%	15/10-B01-325474	2
Caelo	Isosorbide dinitrate 40%	15-10b01-328132	1
Caelo	Isosorbide dinitrate 40%	15-10-b01-328132	2
Caelo	Isosorbide dinitrate 40%	17c29-b01-347885	4
Caelo	Isosorbide dinitrate 40%	701319-0003	1
Caelo	Isosorbide dinitrate 40%	17C29-B01-347589	1
Caelo	Isosorbide dinitrate 40%	1510-B01-315217	1
Caelo	Isosorbide dinitrate 40%	14D-09-B03-300234	1
Caelo	Isosorbide dinitrate 40%	149168	1
Caelo	Isosorbide dinitrate 40%	17C29-B01-348859	2
Caelo	Isosorbide dinitrate 40%	15I10-B01	1
Caelo	Isosorbide dinitrate 40%	14D09-B03-294281	2
Caelo	Isosorbide dinitrate 40%	15/10-B01-320081	4
Caelo	Isosorbide dinitrate 40%	17C29-B01-339447	1
Caelo	Isosorbide dinitrate 40%	11D12-N01	1
Caelo	Isosorbide dinitrate 40%	11/17-N05	1
ebe a	Isosorbide dinitrate 40%	14D09-B03-294281	1
Ebert-Jacobi	Isosorbide dinitrate 40%	15I10-B01-328132	1
Euro OTC	Isosorbide dinitrate 40%	15I10-B01325474	1
Fagro/Noweda	Isosorbide dinitrate 40%	17C29-B01-335070	1

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Supplier	Substance	Batch	Spectra
Fagron	Isosorbide dinitrate 40%	11117-N05	1
Fagron	Isosorbide dinitrate 40%	15-10-b01-325475	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-328132	2
Fagron	Isosorbide dinitrate 40%	15/10-b01-328132	3
Fagron	Isosorbide dinitrate 40%	17c29-b01-339448	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-339448	2
Fagron	Isosorbide dinitrate 40%	17C29-b01-339448	1
Fagron	Isosorbide dinitrate 40%	11D12-N01	2
Fagron	Isosorbide dinitrate 40%	1309210009	1
Fagron	Isosorbide dinitrate 40%	12C08-N05	2
Fagron	Isosorbide dinitrate 40%	11I17-N05	1
Fagron	Isosorbide dinitrate 40%	9101205	1
Fagron	Isosorbide dinitrate 40%	10D29-N10	1
Fagron	Isosorbide dinitrate 40%	12K14-N02	6
Fagron	Isosorbide dinitrate 40%	2413Q03516	1
Fagron	Isosorbide dinitrate 40%	13d15-n02	1
Fagron	Isosorbide dinitrate 40%	11/17-No5	1
Fagron	Isosorbide dinitrate 40%	9E05-N05	1
Fagron	Isosorbide dinitrate 40%	391311-03516	1
Fagron	Isosorbide dinitrate 40%	12K14N02	1
Fagron	Isosorbide dinitrate 40%	10C19-N01	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-294281	3
Fagron	Isosorbide dinitrate 40%	12k14-n02	1
Fagron	Isosorbide dinitrate 40%	101652	4
Fagron	Isosorbide dinitrate 40%	12f08-n04	1
Fagron	Isosorbide dinitrate 40%	14D09-B03_294282	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-294282Eber	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-300234	14
Fagron	Isosorbide dinitrate 40%	testxx	1
Fagron	Isosorbide dinitrate 40%	14-D09-B03-300234	1
Fagron	Isosorbide dinitrate 40%	11F28-N05	2
Fagron	Isosorbide dinitrate 40%	8564340	1
Fagron	Isosorbide dinitrate 40%	14D09-B3-308419	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-313566	3
Fagron	Isosorbide dinitrate 40%	7013190003	1
Fagron	Isosorbide dinitrate 40%	14d09-b03-313566	1
Fagron	Isosorbide dinitrate 40%	14D09-B03_308419	1
Fagron	Isosorbide dinitrate 40%	15I10-B01-318522	1
Fagron	Isosorbide dinitrate 40%	15/10B01-315217	1
Fagron	Isosorbide dinitrate 40%	1510-B01-315217	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-320081	6
Fagron	Isosorbide dinitrate 40%	14D09-B03-305633	1
Fagron	Isosorbide dinitrate 40%	160629I	1
Fagron	Isosorbide dinitrate 40%	15-10-b01-318522	1
Fagron	Isosorbide dinitrate 40%	15I10-B01	7
Fagron	Isosorbide dinitrate 40%	149168	9
Fagron	Isosorbide dinitrate 40%	13F27-N040234/1300	1
Fagron	Isosorbide dinitrate 40%	1510-b01-325475	3
Fagron	Isosorbide dinitrate 40%	1510-B01-320081	1
Fagron	Isosorbide dinitrate 40%	15110-B01-325474	1
Fagron	Isosorbide dinitrate 40%	25021711	1
Fagron	Isosorbide dinitrate 40%	1510-b01-328132	1
Fagron	Isosorbide dinitrate 40%	151-b01-328132	2
Fagron	Isosorbide dinitrate 40%	15/10-B01-328577	5
Fagron	Isosorbide dinitrate 40%	15/10-b01-331287	3
Fagron	Isosorbide dinitrate 40%	15-10-b01-331287	5
Fagron	Isosorbide dinitrate 40%	15/10-B01-331286	4
Fagron	Isosorbide dinitrate 40%	17c29-b01-335071	6
Fagron	Isosorbide dinitrate 40%	15110-B01-331286	1
Fagron	Isosorbide dinitrate 40%	193469	8

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Supplier	Substance	Batch	Spectra
Fagron	Isosorbide dinitrate 40%	17C29-B01335070	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-335071	1
Fagron	Isosorbide dinitrate 40%	17C29B01335070	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-346333	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-348859	13
Fagron	Isosorbide dinitrate 40%	17c29-b01-348859	2
Fagron	Isosorbide dinitrate 40%	17C29-B01-350469	11
Fagron	Isosorbide dinitrate 40%	17c29-b01-350469	1
Fagron	Isosorbide dinitrate 40%	17C29-B01_350469	1
Fagron	Isosorbide dinitrate 40%	1934469	1
Fagron	Isosorbide dinitrate 40%	18J18-B01359579	1
Fagron	Isosorbide dinitrate 40%	18J18-B01-358241	11
Fagron	Isosorbide dinitrate 40%	18J18B01358242	1
Fagron	Isosorbide dinitrate 40%	18-18-b01-358242	2
Fagron	Isosorbide dinitrate 40%	1818b01359178	5
Fagron	Isosorbide dinitrate 40%	18J18-B01	1
Fagron	Isosorbide dinitrate 40%	18J18-B01-359177	2
Fagron	Isosorbide dinitrate 40%	195293	1
Fagron	Isosorbide dinitrate 40%	14D09B03300235	1
Fagron	Isosorbide dinitrate 40%	17c9-b01-347589	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-353161	2
Fagron	Isosorbide dinitrate 40%	15I10-B01-320782	1
Fagron	Isosorbide dinitrate 40%	18J18-B01-359178	1
Fagron	Isosorbide dinitrate 40%	18J18-B01-358247	5
Fagron	Isosorbide dinitrate 40%	15I10-B01-328577	1
Fagron	Isosorbide dinitrate 40%	17C-B01-347589	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-294280	8
Fagron	Isosorbide dinitrate 40%	14D09-B03-29481	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-331287	1
Fagron	Isosorbide dinitrate 40%	11J17-N05	2
Fagron	Isosorbide dinitrate 40%	15I10-B01-320081	5
Fagron	Isosorbide dinitrate 40%	17C29B01347589	1
Fagron	Isosorbide dinitrate 40%	18J18B01-363845	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-335070	10
Fagron	Isosorbide dinitrate 40%	2114M3516	1
Fagron	Isosorbide dinitrate 40%	517I-03516	1
Fagron	Isosorbide dinitrate 40%	17V29-B01-347589	1
Fagron	Isosorbide dinitrate 40%	14D09B03294281	1
Fagron	Isosorbide dinitrate 40%	14D09-B03-307018	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-325474	2
Fagron	Isosorbide dinitrate 40%	17C29-B01	4
Fagron	Isosorbide dinitrate 40%	10029-N10	1
Fagron	Isosorbide dinitrate 40%	P11008	1
Fagron	Isosorbide dinitrate 40%	15I10-B01-328132	1
Fagron	Isosorbide dinitrate 40%	15I10-B01-320081	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-347248	3
Fagron	Isosorbide dinitrate 40%	3413U03516	1
Fagron	Isosorbide dinitrate 40%	13A07-0003	1
Fagron	Isosorbide dinitrate 40%	13I26-N18	10
Fagron	Isosorbide dinitrate 40%	14D09-B03	8
Fagron	Isosorbide dinitrate 40%	14D09-B03-308419	14
Fagron	Isosorbide dinitrate 40%	1510-B01320081	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-347589	8
Fagron	Isosorbide dinitrate 40%	15I10-B01-315217	2
Fagron	Isosorbide dinitrate 40%	18J18_B01_358247	1
Fagron	Isosorbide dinitrate 40%	X12010	1
Fagron	Isosorbide dinitrate 40%	1216M-03516	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-315217	4
Fagron	Isosorbide dinitrate 40%	15I10-B01-310081	1
Fagron	Isosorbide dinitrate 40%	1510B01325474	1

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Supplier	Substance	Batch	Spectra
Fagron	Isosorbide dinitrate 40%	15/10-B10-331286	1
Fagron	Isosorbide dinitrate 40%	17C29-801-347885	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-348860	1
Fagron	Isosorbide dinitrate 40%	17C29-B01-352558	2
Fagron	Isosorbide dinitrate 40%	17c29-B01-48859	1
Fagron	Isosorbide dinitrate 40%	3211U-03516	1
Fagron	Isosorbide dinitrate 40%	4314U-03516	1
Fagron	Isosorbide dinitrate 40%	3115M-03516	1
Fagron	Isosorbide dinitrate 40%	15/10-B01-325474	1
Fagron	Isosorbide dinitrate 40%	17c29-b01	1
Fagron	Isosorbide dinitrate 40%	17C29B01339447	1
Fagron	Isosorbide dinitrate 40%	11/17-N05	1
Fagron	Isosorbide dinitrate 40%	13F27-N04	6
Fagron	Isosorbide dinitrate 40%	14D09-B03-294282	3
Fagron	Isosorbide dinitrate 40%	15I10-B01-325474	6
Fargon	Isosorbide dinitrate 40%	15/10-B01-320081	1
Fargon	Isosorbide dinitrate 40%	17C29-B01	1
Fargon/Gehe	Isosorbide dinitrate 40%	17C29-B01-339447	1
Fiebig	Isosorbide dinitrate 40%	17C29-B01-350469	1
Fiebig 23.05.13 ek: 10,...	Isosorbide dinitrate 40%	12F08-N04	1
Frago/Gehe	Isosorbide dinitrate 40%	17C29-B01-335070	1
Frago/Noweda	Isosorbide dinitrate 40%	15I10-B01-328577	1
Gehe	Isosorbide dinitrate 40%	18J18-B01-358241	1
GEHE	Isosorbide dinitrate 40%	17C29-B01-347589	1
Caelo	Isosorbide dinitrate 40%	193469	1
Fagron	Isosorbide dinitrate 40%	1510B01320081	1
Fagron	Isosorbide dinitrate 40%	1510B01328577	1
Ichthyol-Gesellschaft	Isosorbide dinitrate 40%	17C29-B01-335070	1
Krieger	Isosorbide dinitrate 40%	3186	1
L12	Isosorbide dinitrate 40%	149168	1
L12	Isosorbide dinitrate 40%	15I10-B01-331286	2
Noweda	Isosorbide dinitrate 40%	15/10-B01-315217	1
Caelo	Isosorbide dinitrate 40%	14D09-B03-308419	3
Phoenix	Isosorbide dinitrate 40%	3066	1
Phoenix	Isosorbide dinitrate 40%	3362	1
Phönix	Isosorbide dinitrate 40%	13A07-N13	1
Sanacorp	Isosorbide dinitrate 40%	11J17-N05	1
Sanacorp	Isosorbide dinitrate 40%	14D09-B03-294280	1
Sanacorp	Isosorbide dinitrate 40%	193469	1
Caelo	Isosorbide dinitrate 40%	17C29-B01-348860	1
VDL	Isosorbide dinitrate 40%	18J18-B01-358247	1
Wepa	Isosorbide dinitrate 40%	14D09-B03-313566	1
Euro OTC	Isosorbide dinitrate 40%		1
	Isosorbide dinitrate 40%	17c29-b01-348859	1
Fagron	Isosorbide dinitrate 40%	12F08-N04	8
Fagron	Isosorbide dinitrate 40%	13D15-N02	7
Fagron	Isosorbide dinitrate 40%	15I10-B01-328577	2
Fagron	Isosorbide dinitrate 40%	17C29-B01-339447	7
Fagron	Isosorbide dinitrate 40%		4
VDI 28.10.14 10,32 euro	Isosorbide dinitrate 40%		1

- 110 792 spectra from 742 *Apo-Ident* customers from a total of 31 730 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Isosorbide dinitrate 40%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isosorbide dinitrate 40%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	189	0	110 500
Type B	0	80	0	119 062
Type C	0	454	1	110 792

The substance/substance group *Isosorbide dinitrate 40%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.8254 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	99.7802 % (> 99.1209 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Isosorbide dinitrate 40%* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fructose	37.55	—
Levothyroxin sodium	42.89	—
Sodium acetate trihydrate	45.08	—
Magnesium citrate	46.12	—
Calcium glycerophosphate	46.90	—
Aciclovir	49.68	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Isosorbide dinitrate 40%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20891	23200	8.40	20.54
21347	23200	5.25	21.15
23200	23200	0.00	21.90
23598	23200	5.00	22.02
24057	23200	8.33	22.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Isoxuprine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22640-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Isoxuprine hydrochloride; Isoxsuprini hydrochloridum

Special notes

When selecting the *Isoxuprine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Isoxuprine hydrochloride	5	1	0

Second-stage model

For differentiation of the substance/substance group *Isoxuprine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Isoxuprine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Isoxuprine hydro...	161770	22640	40	20160818*
Caelo	Isoxuprine hydro...	16177001	22735	40	20160818
Caelo	Isoxuprine hydro...	181078	24252	40	20180719*
Euro OTC	Isoxuprine hydro...	1503008-01	22659	40	20150430
Euro OTC	Isoxuprine hydro...	1905019	24920	40	20191128*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Isoxuprine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 489 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Isoxuprine hydrochloride*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Isoxuprine hydrochloride	190117	24547	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Isoxuprine hydrochloride*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Isoxuprine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Isoxuprine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Isoxuprine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Isoxuprine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fampridine	31.14	—
Eosin Y	45.73	—
Sodium cromoglicate	48.32	—
Oxytetracycline hydrochloride	49.23	—
Quinine sulfate	54.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Isoxuprine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22640	22640	0.00	43.86
22659	22640	2.54	44.29
22735	22640	2.32	45.01
24252	24252	0.00	43.64
24920	24920	0.00	42.65

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ketamine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20278-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ketamine hydrochloride; Ketamini hydrochloridum

Special notes

When selecting the *Ketamine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ketamine hydrochloride	3	2	20

Second-stage model

For differentiation of the substance/substance group *Ketamine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ketamine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ketamine hydroch. . .	13H19-N01	21044	40	8931
Fagron	Ketamine hydroch. . .	14I03-B02-303165	21779	60	20140926
Fagron	Ketamine hydroch. . .	14I03-B02-311706	22533	40	20140926

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Ketamine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Ketamine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ketamine hydrochloride	15E07-B03-322164	23201	40
Fagron	Ketamine hydrochloride	16E18-B03-339897	23941	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 30 spectra from 19 *Apo-Ident* customers from 22 batches from the substance/substance group *Ketamine hydrochloride*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Ketamine hydrochloride	182513P	1
Fagron	Ketamine hydrochloride	14/03-B02-303165	1
Fagron	Ketamine hydrochloride	15E07-B03-322164	5
Fagron	Ketamine hydrochloride	16E18-B03-332957	1
Fagron	Ketamine hydrochloride	16E18-B03	1
Fagron	Ketamine hydrochloride	16E18-B03-334370	1
Fagron	Ketamine hydrochloride	17K14-B01-347996	3
Fagron	Ketamine hydrochloride	19h14-f02-364305	1
Fagron	Ketamine hydrochloride	173017P	1
Fagron	Ketamine hydrochloride	17K14-B01-356831	1
Fagron	Ketamine hydrochloride	17K14-B01-347995	2
Fagron	Ketamine hydrochloride	17K14-B01-358396	1
Fagron	Ketamine hydrochloride	14I03-B02-309852	1
Fagron	Ketamine hydrochloride	16E18-B03-328264	1
Fagron	Ketamine hydrochloride	16E18-B03-339897	2
Fagron	Ketamine hydrochloride	17K14-B01-3533344	1
Gatt-Koller	Ketamine hydrochloride	1803056	1
GEHE 27.05.2014	Ketamine hydrochloride	13H19-N01	1
Noweda	Ketamine hydrochloride	14/03-B02-311706	1
Noweda	Ketamine hydrochloride	292414P	1
phönix	Ketamine hydrochloride	14I03-B02-311706	1
Fagron	Ketamine hydrochloride	14I03-B02-303165	1

- 111217 spectra from 742 *Apo-Ident* customers from a total of 31869 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ketamine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ketamine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	29	1	111 217

The substance/substance group *Ketamine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	96.6667 % (> 86.6667 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ketamine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tetracaine hydrochloride	45.70	—
Omeprazole	48.84	—
Ibuprofen	53.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ketamine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22533	21044	3.83	64.91
21044	21044	0.00	64.96
21779	21044	2.49	64.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ketoconazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20688-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ketoconazole; Ketoconazolum

Special notes

When selecting the *Ketoconazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ketoconazole	5	1	51

Second-stage model

For differentiation of the substance/substance group *Ketoconazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ketoconazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ketoconazole	12171007	20688	30	1401554
Caelo	Ketoconazole	13179612	21514	60	20130613
Caelo	Ketoconazole	13179612	21515	60	20130613
Caelo	Ketoconazole	153477	24028	40	20151113*
Fagron	Ketoconazole	12A16-N06	20699	40	20120123
Fagron	Ketoconazole	16A26-B01-322982	23183	40	20160210

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 270 spectra of 6 reference samples from the substance/substance group *Ketoconazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 419 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Ketoconazole*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ketoconazole	17H14-B01-339422	23917	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 117 spectra from 65 *Apo-Ident* customers from 53 batches from the substance/substance group *Ketoconazole*.
- Among them are spectra of independent samples from 51 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ANZAG 23.07.14	Ketoconazole	13h09-n07	1
Caelo	Ketoconazole	11070022	1
Caelo	Ketoconazole	12300406	1
Caelo	Ketoconazole	13399404	8
Caelo	Ketoconazole	14350427	2
Caelo	Ketoconazole	14350437	5
Caelo	Ketoconazole	14k04-b06-309671	1
Caelo	Ketoconazole	18007011	3
Caelo	Ketoconazole	13399412	1
Caelo	Ketoconazole	18007015	2
Caelo	Ketoconazole	13179601	2
Caelo	Ketoconazole	13399408	6
Caelo	Ketoconazole	14350408	2
Caelo	Ketoconazole	18007003	3
Caelo	Ketoconazole	18007020	2
Caelo	Ketoconazole	14350416	3
Caelo	Ketoconazole	13179606	3
Caelo	Ketoconazole	14350419	1
Caelo	Ketoconazole	14350429	5
Caelo	Ketoconazole	19096601	1
Caelo	Ketoconazole	1906611	1
Caelo	Ketoconazole	14350434	1
Caelo	Ketoconazole	14350436	2
Caelo	Ketoconazole	15347701	10
Caelo	Ketoconazole	53317046	2
Caelo	Ketoconazole	14350421	1
Caelo	Ketoconazole	14350422	3
Caelo	Ketoconazole	14350420	2
Caelo	Ketoconazole	14350442	3
Caelo /Gehe	Ketoconazole	14350408	1
Caesar & Loretz GmbH / ...	Ketoconazole	19096601	1
E Plus	Ketoconazole	14350429	1
Euro OTC	Ketoconazole	13179615	1
Fagron	Ketoconazole	5015E-02866	1
Fagron	Ketoconazole	12I17-N02	1
Fagron	Ketoconazole	13J23-N04	1
Fagron	Ketoconazole	13179613	1

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Supplier	Substance	Batch	Spectra
Fagron	Ketoconazole	14E09-B01-297637	2
Fagron	Ketoconazole	14E09-B01-293736	3
Fagron	Ketoconazole	15G23-B03-312063	1
Fagron	Ketoconazole	15G23-B03-316596	1
Fagron	Ketoconazole	16A26-B01-327490	1
Fagron	Ketoconazole	17H14-B01-344222	1
Fagron	Ketoconazole	17H14-B01-353376	1
Fagron	Ketoconazole	18E28-B02-364169	1
Fagron	Ketoconazole	13H09-N07	1
Fagron	Ketoconazole	14K04-B06-309671	2
Fagron	Ketoconazole	16A26-B01-335467	2
Fagron	Ketoconazole	KET/11707237	1
Fagron	Ketoconazole	17H14-B01-339422	1
Fiebig	Ketoconazole	14350437	1
Fiebig	Ketoconazole	19096601	1
Gehe	Ketoconazole	11070019	1
Caelo	Ketoconazole	12300407	2
Phoenix	Ketoconazole	19096601	1
Phönix	Ketoconazole	12171018	1
Phönix	Ketoconazole	13179602	3
Caelo	Ketoconazole	11070001	1
Caelo	Ketoconazole	13179612	2

- 111 130 spectra from 742 *Apo-Ident* customers from a total of 31 838 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ketoconazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ketoconazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	270	0	110 419
Type B	0	40	0	119 102
Type C	0	117	0	111 130

The substance/substance group *Ketoconazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.7778 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 94.8718 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ketoconazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	55.10	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ketoconazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20688	20688	0.00	74.52
20699	24028	5.17	76.01
21514	24028	8.18	75.64
21515	24028	9.15	75.43
23183	24028	9.60	73.48
24028	24028	0.00	75.66

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Lactose monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20029-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lactose monohydrate; Lactosum monohydricum

Special notes

When selecting the *Lactose monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lactose monohydrate	6	5	398

Second-stage model

For differentiation of the substance/substance group *Lactose monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lactose monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Lactose monohydr...	12139910	20685	30	20120606
Caelo	Lactose monohydr...	14025601	21525	40	20140207
Caelo	Lactose monohydr...	14025601	21526	40	20140207
Caelo	Lactose monohydr...	14025601	21527	40	20140207
Caelo	Lactose monohydr...	14025601	21528	40	20140207
Caelo	Lactose monohydr...	14025601	21529	40	20140207
Caelo	Lactose monohydr...	160277	22460	60	20160321*
Euro OTC	Lactose monohydr...	1509030	21935	60	20151013*
Euro OTC	Lactose monohydr...	1606025	22701	40	20160628*
Euro OTC	Lactose monohydr...	1909014	24929	40	20191015*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 430 spectra of 10 reference samples from the substance/substance group *Lactose monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 259 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 200 spectra of 5 reference samples from the substance/substance group *Lactose monohydrate*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Lactose monohydrate	15236220	22584	40
Caelo	Lactose monohydrate	173360	23828	40
Euro OTC	Lactose monohydrate	1703019	23141	40
Euro OTC	Lactose monohydrate	1802002	23962	40
Euro OTC	Lactose monohydrate	1812008	24415	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1262 spectra from 329 *Apo-Ident* customers from 402 batches from the substance/substance group *Lactose monohydrate*.
- Among them are spectra of independent samples from 399 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H.D.	Lactose monohydrate	12336801	1
AEP	Lactose monohydrate	18198007	2
AHD	Lactose monohydrate	13I23-B03-291114	1
Alliance Healthcare	Lactose monohydrate	10195101	2
Caelo	Lactose monohydrate	18198001	11
Alte Apotheke	Lactose monohydrate	16027708	1
Anzag	Lactose monohydrate	12139915	5
Anzag / Noweda	Lactose monohydrate	12336815	1
Anzag 29.11.12 ek:7,51	Lactose monohydrate	12139914	1
Anzag/Fragon	Lactose monohydrate	1005SLP	1
Bahnhof-Apotheke	Lactose monohydrate	120614	1
Bahnhof-Apotheke	Lactose monohydrate	120808	1
Bahnhof-Apotheke	Lactose monohydrate	121119	2
Bahnhof-Apotheke	Lactose monohydrate	130115	1
Bahnhof-Apotheke	Lactose monohydrate	130729	1
Bahnhof-Apotheke	Lactose monohydrate	130911	1
Bahnhof-Apotheke	Lactose monohydrate	130925	1
Bahnhof-Apotheke	Lactose monohydrate	131023	1
Bahnhof-Apotheke	Lactose monohydrate	131112	1
Bahnhof-Apotheke	Lactose monohydrate	131127	2
Bahnhof-Apotheke	Lactose monohydrate	131218	2
Bahnhof-Apotheke	Lactose monohydrate	140113	3
Bahnhof-Apotheke	Lactose monohydrate	140206	2
Bahnhof-Apotheke	Lactose monohydrate	140310	2
Bahnhof-Apotheke	Lactose monohydrate	140220	1
Bahnhof-Apotheke	Lactose monohydrate	140630	1

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Supplier	Substance	Batch	Spectra
Bahnhoofsapotheke	Lactose monohydrate	140401	1
Bären Apotheke	Lactose monohydrate	16231206	1
Bombastus	Lactose monohydrate	13299108	1
Bombastus	Lactose monohydrate	275194/0	1
Bombastus	Lactose monohydrate	275225/0	1
Bombastus	Lactose monohydrate	272680/0	1
Bombastus	Lactose monohydrate	274926	1
Bombastus	Lactose monohydrate	283992	2
Bombastus	Lactose monohydrate	282648	1
Bombastus	Lactose monohydrate	284321/0	1
Bombastus	Lactose monohydrate	282696/0	1
Bombastus	Lactose monohydrate	286697/0	1
Bombastus	Lactose monohydrate	285087/0	1
Bombastus	Lactose monohydrate	288015/0	1
Bombastus	Lactose monohydrate	288927	1
Bombastus	Lactose monohydrate	289238	1
Bombastus	Lactose monohydrate	291464	1
Bombastus	Lactose monohydrate	294897/0	1
Bombastus	Lactose monohydrate	294184/0	1
Bombastus	Lactose monohydrate	295011/0	1
Bombastus	Lactose monohydrate	293918/0	1
Bombastus	Lactose monohydrate	306147	3
Bombastus	Lactose monohydrate	305227	2
Bombastus	Lactose monohydrate	3020165	1
Bombastus	Lactose monohydrate	293289	1
Bombastus	Lactose monohydrate	304755	1
Bombastus	Lactose monohydrate	300657	2
Bombastus	Lactose monohydrate	303658	2
Bombastus	Lactose monohydrate	2932880	1
Bombastus	Lactose monohydrate	295715	1
Bombastus	Lactose monohydrate	293649	1
Bombastus	Lactose monohydrate	295476	1
Bombastus	Lactose monohydrate	293970	1
Bombastus	Lactose monohydrate	295714	1
Bombastus	Lactose monohydrate	293074	1
Bombastus	Lactose monohydrate	292996	1
Bombastus	Lactose monohydrate	292995	1
Bombastus	Lactose monohydrate	286710	1
Bombastus	Lactose monohydrate	286354	1
Bombastus	Lactose monohydrate	294154	1
Bombastus	Lactose monohydrate	292983	1
Bombastus	Lactose monohydrate	293290	1
Bombastus	Lactose monohydrate	292982	2
Bombastus	Lactose monohydrate	305336	2
Bombastus	Lactose monohydrate	306850	1
Bombastus	Lactose monohydrate	306652	1
Bombastus	Lactose monohydrate	306990	1
Bombastus	Lactose monohydrate	306964	1
Bombastus	Lactose monohydrate	306651/0	1
Bombastus	Lactose monohydrate	305227/0	1
Bombastus	Lactose monohydrate	305336/0	1
Bombastus	Lactose monohydrate	307573/0	1
Bombastus	Lactose monohydrate	306989	2
Bombastus	Lactose monohydrate	307741	1
Bombastus	Lactose monohydrate	307543	2
Bombastus	Lactose monohydrate	3077410	1
Bombastus	Lactose monohydrate	308118/0	1
Bombastus	Lactose monohydrate	307976/0	1
Bombastus	Lactose monohydrate	307702/0	1
Bombastus	Lactose monohydrate	307444/0	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Lactose monohydrate	309508	1
Bombastus	Lactose monohydrate	308438	1
Bombastus	Lactose monohydrate	309351	1
Bombastus	Lactose monohydrate	309413/0	1
Bombastus	Lactose monohydrate	308117	1
Bombastus	Lactose monohydrate	309509	1
Bombastus	Lactose monohydrate	311280/0	1
Bombastus	Lactose monohydrate	308117/0	1
Bombastus	Lactose monohydrate	310691/0	1
Bombastus	Lactose monohydrate	311362/0	1
Bombastus	Lactose monohydrate	309509/0	1
Bombastus	Lactose monohydrate	310912/0	1
Bombastus	Lactose monohydrate	310082/0	1
Bombastus	Lactose monohydrate	310905/0	1
Bombastus	Lactose monohydrate	310691	1
Bombastus	Lactose monohydrate	311280	1
Bombastus	Lactose monohydrate	17000754	1
Bombastus	Lactose monohydrate	17001199	1
Bombastus	Lactose monohydrate	310905	1
Bombastus	Lactose monohydrate	17001212	1
Caelo	Lactose monohydrate	7111402	1
Caelo	Lactose monohydrate	11079002	2
Caelo	Lactose monohydrate	11219216	2
Caelo	Lactose monohydrate	12021508	1
Caelo	Lactose monohydrate	12021518	5
Caelo	Lactose monohydrate	30101201	1
Caelo	Lactose monohydrate	1106022-02	1
Caelo	Lactose monohydrate	17011301	1
Caelo	Lactose monohydrate	2901312210	1
Caelo	Lactose monohydrate	11014714	1
Caelo	Lactose monohydrate	12139920	6
Caelo	Lactose monohydrate	1301C005	2
Caelo	Lactose monohydrate	12336801	7
Caelo	Lactose monohydrate	12336815	9
Caelo	Lactose monohydrate	s-100513-1	1
Caelo	Lactose monohydrate	1071302	1
Caelo	Lactose monohydrate	13104902	7
Caelo	Lactose monohydrate	13081302	1
Caelo	Lactose monohydrate	13104901	5
Caelo	Lactose monohydrate	6091301	1
Caelo	Lactose monohydrate	C1023	1
Caelo	Lactose monohydrate	13104910	2
Caelo	Lactose monohydrate	24011405	1
Caelo	Lactose monohydrate	8021401	1
Caelo	Lactose monohydrate	20021411	1
Caelo	Lactose monohydrate	7031402	1
Caelo	Lactose monohydrate	12399107	1
Caelo	Lactose monohydrate	12041401	1
Caelo	Lactose monohydrate	9051401	1
Caelo	Lactose monohydrate	14025604	6
Caelo	Lactose monohydrate	140612	3
Caelo	Lactose monohydrate	26071401	1
Caelo	Lactose monohydrate	3091405	1
Caelo	Lactose monohydrate	1402504	1
Caelo	Lactose monohydrate	14025620	11
Caelo	Lactose monohydrate	23101404	1
Caelo	Lactose monohydrate	14140305	8
Caelo	Lactose monohydrate	3121406	1
Caelo	Lactose monohydrate	14025619	3
Caelo	Lactose monohydrate	3031501	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lactose monohydrate	14333503	1
Caelo	Lactose monohydrate	14333502	2
Caelo	Lactose monohydrate	30031503	1
Caelo	Lactose monohydrate	200415HJK02	1
Caelo	Lactose monohydrate	14333508	1
Caelo	Lactose monohydrate	14333511	5
Caelo	Lactose monohydrate	23051501	1
Caelo	Lactose monohydrate	5061504	1
Caelo	Lactose monohydrate	14333513	7
Caelo	Lactose monohydrate	23061504	1
Caelo	Lactose monohydrate	8071501	1
Caelo	Lactose monohydrate	14333521	8
Caelo	Lactose monohydrate	14333514	1
Caelo	Lactose monohydrate	15236204	10
Caelo	Lactose monohydrate	15236203	4
Caelo	Lactose monohydrate	14333528	2
Caelo	Lactose monohydrate	15236208	11
Caelo	Lactose monohydrate	15236214	8
Caelo	Lactose monohydrate	15236209	9
Caelo	Lactose monohydrate	15236215	4
Caelo	Lactose monohydrate	1433520	1
Caelo	Lactose monohydrate	15236202	1
Caelo	Lactose monohydrate	1523614	1
Caelo	Lactose monohydrate	16027702	6
Caelo	Lactose monohydrate	152362	2
Caelo	Lactose monohydrate	16027706	5
Caelo	Lactose monohydrate	16027704	1
Caelo	Lactose monohydrate	150903002	1
Caelo	Lactose monohydrate	16027701	3
Caelo	Lactose monohydrate	123Test	1
Caelo	Lactose monohydrate	123456test	1
Caelo	Lactose monohydrate	12345test	1
Caelo	Lactose monohydrate	1234test	1
Caelo	Lactose monohydrate	16231207	9
Caelo	Lactose monohydrate	123456	1
Caelo	Lactose monohydrate	16231208	5
Caelo	Lactose monohydrate	Testmessung	1
Caelo	Lactose monohydrate	5041702	1
Caelo	Lactose monohydrate	16231206	5
Caelo	Lactose monohydrate	2051702	1
Caelo	Lactose monohydrate	10071701	1
Caelo	Lactose monohydrate	16231212	8
Caelo	Lactose monohydrate	15081701	1
Caelo	Lactose monohydrate	16091710	1
Caelo	Lactose monohydrate	6101702	1
Caelo	Lactose monohydrate	17078307	4
Caelo	Lactose monohydrate	17078302	6
Caelo	Lactose monohydrate	27101702	1
Caelo	Lactose monohydrate	162312135465	1
Caelo	Lactose monohydrate	17321004	8
Caelo	Lactose monohydrate	11041801	1
Caelo	Lactose monohydrate	17321002	3
Caelo	Lactose monohydrate	9061803	1
Caelo	Lactose monohydrate	17336005	7
Caelo	Lactose monohydrate	26061801	1
Caelo	Lactose monohydrate	17336002	7
Caelo	Lactose monohydrate	21071801	1
Caelo	Lactose monohydrate	17336009	6
Caelo	Lactose monohydrate	17336007	28
Caelo	Lactose monohydrate	30081801	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lactose monohydrate	21111813	1
Caelo	Lactose monohydrate	2011901	1
Caelo	Lactose monohydrate	5011901	1
Caelo	Lactose monohydrate	1733609	1
Caelo	Lactose monohydrate	1733008	1
Caelo	Lactose monohydrate	18198016	5
Caelo	Lactose monohydrate	16231202	16
Caelo	Lactose monohydrate	16027703	6
Caelo	Lactose monohydrate	14140302	4
Caelo	Lactose monohydrate	123test	1
Caelo	Lactose monohydrate	1703019-01	3
Caelo	Lactose monohydrate	17336008	12
Caelo	Lactose monohydrate	18198007	9
Caelo	Lactose monohydrate	14140308	7
Caelo	Lactose monohydrate	10195107	2
Caelo	Lactose monohydrate	1433502	1
Caelo	Lactose monohydrate	17078306	9
Caelo	Lactose monohydrate	11219208	3
Caelo	Lactose monohydrate	12139914	6
Caelo	Lactose monohydrate	12336816	3
Caelo	Lactose monohydrate	13104911	2
Caelo	Lactose monohydrate	13299107	5
Caelo	Lactose monohydrate	14025603	7
Caelo	Lactose monohydrate	14333501	3
Caelo	Lactose monohydrate	14333509	10
Caelo	Lactose monohydrate	16231203	4
Caelo	Lactose monohydrate	1509030-02	1
Caelo	Lactose monohydrate	18198008	4
Caelo	Lactose monohydrate	13299101	9
Caelo	Lactose monohydrate	14140312	13
Caelo	Lactose monohydrate	18198013	1
Caelo	Lactose monohydrate	13104909	5
Caelo	Lactose monohydrate	3295	1
Caelo	Lactose monohydrate	16321202	1
Caelo	Lactose monohydrate	17336013	7
Caelo	Lactose monohydrate	18198006	3
Caelo	Lactose monohydrate	12021502	1
Caelo	Lactose monohydrate	112192	2
Caelo	Lactose monohydrate	13104909-3422310182	1
Caelo	Lactose monohydrate	13104909-3453311172	1
Caelo	Lactose monohydrate	1401003-01	1
Caelo	Lactose monohydrate	18198017	2
Caelo	Lactose monohydrate	15236217	1
Caelo	Lactose monohydrate	16027707	2
Caelo	Lactose monohydrate	19137601	4
Caelo	Lactose monohydrate	17078303	25
Caelo	Lactose monohydrate	12139909	1
Caelo	Lactose monohydrate	12336814	1
Caelo	Lactose monohydrate	13299103	1
Caelo	Lactose monohydrate	14025616	3
Caelo	Lactose monohydrate	14140304	2
Caelo	Lactose monohydrate	14140309	2
Caelo	Lactose monohydrate	15236201	22
Caelo	Lactose monohydrate	1433518	2
Caelo	Lactose monohydrate	1090216	1
Caelo	Lactose monohydrate	16231211	20
Caelo	Lactose monohydrate	1623120803815470	1
Caelo	Lactose monohydrate	16231214	5
Caelo	Lactose monohydrate	1802002-01	1
Caelo	Lactose monohydrate	18198014	6

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lactose monohydrate	17078303-20180619Ma2	1
Caelo	Lactose monohydrate	16231215	4
Caelo	Lactose monohydrate	160913PJK01	1
Caelo	Lactose monohydrate	1433510	1
Caelo	Lactose monohydrate	13104908	2
Caelo	Lactose monohydrate	12139908	1
Caelo	Lactose monohydrate	12336820	2
Caelo	Lactose monohydrate	12139912	1
Caelo	Lactose monohydrate	13104912	1
Caelo	Lactose monohydrate	13299108	5
Caelo	Lactose monohydrate	14333510	1
Caelo	Lactose monohydrate	143335114	1
Caelo	Lactose monohydrate	15236220	4
Caelo	Lactose monohydrate	14025615	1
Caelo	Lactose monohydrate	16231213	2
Caelo	Lactose monohydrate	1703019-020	1
Caelo	Lactose monohydrate	17321005	1
Fagron	Lactose monohydrate	1802002-01	1
Caelo	Lactose monohydrate	4313Q2210	1
Caelo	Lactose monohydrate	15011701	1
Caelo	Lactose monohydrate	15236221	6
Caelo	Lactose monohydrate	17078312	17
Caelo	Lactose monohydrate	17321001	23
Caelo	Lactose monohydrate	14333518	4
Caelo	Lactose monohydrate	1433521	1
Caelo	Lactose monohydrate	1526201	1
Caelo	Lactose monohydrate	16027708	8
Caelo	Lactose monohydrate	16231201	5
Caelo	Lactose monohydrate	17336014	6
Caelo	Lactose monohydrate	18198002	4
Caelo	Lactose monohydrate	1501017-01	4
Caelo	Lactose monohydrate	13299102	12
Caelo	Lactose monohydrate	14025608	2
Caelo	Lactose monohydrate	14333520	10
Caelo	Lactose monohydrate	15236213	2
Caelo	Lactose monohydrate	18198003	1
Caelo	Lactose monohydrate	3788916	1
Caeo/Noweda	Lactose monohydrate	1523204	1
Caesar & Loretz GmbH	Lactose monohydrate	14140311	1
Caesar & Loretz GmbH	Lactose monohydrate	17336007	1
Caesar & Loretz GmbH	Lactose monohydrate	18198006	1
Caesar & Loretz GmbH	Lactose monohydrate	18198002	8
Caesar & Loretz GmbH	Lactose monohydrate	18198001	4
Caesar & Loretz GmbH	Lactose monohydrate	18198014	3
Caesar & Loretz GmbH	Lactose monohydrate	19137601	1
Caesar & Loretz GmbH	Lactose monohydrate	18198023	1
Caesar & Loretz GmbH / ...	Lactose monohydrate	18198006	1
Caesar & Loretz GmbH/Ge...	Lactose monohydrate	18198014	1
Caesar & Loretz GmbH/Gö...	Lactose monohydrate	18198007	1
Caesar & Loretz GmbH/No...	Lactose monohydrate	18198007	1
Caesar & Loretz/Noweda	Lactose monohydrate	15236204	1
Caesar /phönix	Lactose monohydrate	13104901	2
Caesar u Loretz	Lactose monohydrate	1433520	1
Caesar u Loretz	Lactose monohydrate	16231202	1
Caesar u. Loretz	Lactose monohydrate	14025620	1
Cealo	Lactose monohydrate	13104901	1
Cealo	Lactose monohydrate	16231202	1
Celo/Kehr	Lactose monohydrate	16231213	2
cesar&lorenz/Phönix	Lactose monohydrate	12336815	1
Chiesi	Lactose monohydrate	16027708	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Ebert u. Jacobi 18.0...	Lactose monohydrate	15236215	1
Edelweiss	Lactose monohydrate	253292176-1124	1
Edelweiss/Geibo	Lactose monohydrate	258710315-1203	1
Eigenherstellung	Lactose monohydrate	40113HJK01	1
Eigenherstellung	Lactose monohydrate	70113HML01	1
Eigenherstellung	Lactose monohydrate	110913HJK01	1
Eigenherstellung	Lactose monohydrate	60814HSA01	1
Eigenherstellung	Lactose monohydrate	40815HMS01	1
EuRho	Lactose monohydrate	1112020-01	1
EuRho	Lactose monohydrate	1112020-02	2
EuRho	Lactose monohydrate	1301028-01	1
EuRho	Lactose monohydrate	1501017-01	1
EuRho	Lactose monohydrate	1509030-02	1
EuRho	Lactose monohydrate	170301901	3
Euro OCT	Lactose monohydrate	1401003-01	3
Euro OTC	Lactose monohydrate	L101854417A545	1
Euro OTC	Lactose monohydrate	L101852618	1
Euro OTC	Lactose monohydrate	1812008-01	1
Euro OTC	Lactose monohydrate	1301028-01	8
Euro OTC	Lactose monohydrate	1301028-02	12
Euro OTC	Lactose monohydrate	140-1003-01	1
Euro OTC	Lactose monohydrate	1501017-01	11
Euro OTC	Lactose monohydrate	1501017-02	1
Euro OTC	Lactose monohydrate	15010	1
Euro OTC	Lactose monohydrate	1301028-03	2
Euro OTC	Lactose monohydrate	160602501	1
Euro OTC	Lactose monohydrate	1802002-01	6
Euro OTC	Lactose monohydrate	1112020-02	4
Euro OTC	Lactose monohydrate	1112020-01	2
Euro OTC	Lactose monohydrate	130102801	1
Euro OTC	Lactose monohydrate	31102013A	1
Euro OTC	Lactose monohydrate	1401003-01	10
Euro OTC	Lactose monohydrate	18082014A	1
Euro OTC	Lactose monohydrate	14025604	2
Euro OTC	Lactose monohydrate	1401003	1
Euro OTC	Lactose monohydrate	1703019-02	4
Euro OTC	Lactose monohydrate	1606025-02	3
Euro OTC	Lactose monohydrate	1812008-03	1
Euro OTC	Lactose monohydrate	1606025-01	28
Euro OTC	Lactose monohydrate	110602202	1
Euro OTC	Lactose monohydrate	3215A-02210	1
Euro OTC	Lactose monohydrate	5123	1
Euro OTC	Lactose monohydrate	17A11-B01-334251	1
Euro OTC	Lactose monohydrate	14025616	2
Euro OTC	Lactose monohydrate	15090-30-02	1
Euroo/Phoenix	Lactose monohydrate	1401003-02	1
Euro OTC	Lactose monohydrate	1509030-01	7
Euro OTC	Lactose monohydrate	UP250171017	1
Euro OTC	Lactose monohydrate	1401003-02	7
Euro OTC	Lactose monohydrate	140100302	1
Euro OTC	Lactose monohydrate	1013Q-02210	1
Euro OTC	Lactose monohydrate	1703019-01	4
Euro OTC	Lactose monohydrate	L1237A4172	2
Europ Ots Pharma	Lactose monohydrate	1301028-02	3
Europ Ots Pharma	Lactose monohydrate	1401003-02	1
Europharm/Otto	Lactose monohydrate	1106022-01	1
Fagron	Lactose monohydrate	11L22-N03	1
Fagron	Lactose monohydrate	12G27-N02	5
Fagron	Lactose monohydrate	12C26-N05	1
Fagron	Lactose monohydrate	11C29-N06	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Lactose monohydrate	1301C007-278131	1
Fagron	Lactose monohydrate	1303C003-280390	1
Fagron	Lactose monohydrate	1301C006-278128	6
Fagron	Lactose monohydrate	12C09-N04	1
Fagron	Lactose monohydrate	1303C003	1
Fagron	Lactose monohydrate	1303C001	1
Fagron	Lactose monohydrate	1303C002-280398	1
Fagron	Lactose monohydrate	13E23-B01	2
Fagron	Lactose monohydrate	282567/0	1
Fagron	Lactose monohydrate	13I23-B03	4
Fagron	Lactose monohydrate	12/23-B02-287554	1
Fagron	Lactose monohydrate	13I23-B03-291115	1
Fagron	Lactose monohydrate	13J23-B03-291114	1
Fagron	Lactose monohydrate	14A30-B07	2
Fagron	Lactose monohydrate	14A30-B07-296182	2
Fagron	Lactose monohydrate	15A19-B06-303437	3
Fagron	Lactose monohydrate	15A19-B06	3
Fagron	Lactose monohydrate	15A19-B06-303439	3
Fagron	Lactose monohydrate	14H27-B02-302033	1
Fagron	Lactose monohydrate	16231215	1
Fagron	Lactose monohydrate	1623123	1
Fagron	Lactose monohydrate	17078302	1
Fagron	Lactose monohydrate	17321001	1
Fagron	Lactose monohydrate	17336007	2
Fagron	Lactose monohydrate	1303C001-280388	1
Fagron	Lactose monohydrate	13E23-B01-283332	2
Fagron	Lactose monohydrate	14140312	1
Fagron	Lactose monohydrate	13I23-B03-291116	1
Fagron	Lactose monohydrate	14H27-B02	1
Fagron	Lactose monohydrate	13/23-B02-287554	1
Fagron	Lactose monohydrate	14H27-B01-305666	1
Fagron	Lactose monohydrate	13E23-B01-283334	1
Fagron	Lactose monohydrate	10751120	1
Fagron	Lactose monohydrate	15H14-B03-314451	3
Fagron	Lactose monohydrate	10726158	1
Fagron	Lactose monohydrate	18B15-B06-353917	1
Fagron	Lactose monohydrate	1301C005-278129	2
Fagron	Lactose monohydrate	14333525	1
Fagron	Lactose monohydrate	13I23-B03-287414	1
Fagron	Lactose monohydrate	18B15-B06-35917	1
Fagron	Lactose monohydrate	14333518	1
Finteler Apotheke	Lactose monohydrate	16231211	1
Fragon	Lactose monohydrate	10706040	1
Gatt-Koller	Lactose monohydrate	1702456	1
Gatt-Koller / Phoenix	Lactose monohydrate	5580/12120813	2
gehe	Lactose monohydrate	16231211	1
Gehe	Lactose monohydrate	1112020-01	1
Gehe	Lactose monohydrate	1112020-02	3
Gehe	Lactose monohydrate	1301028-02	2
Gehe	Lactose monohydrate	16231211	1
Gehe	Lactose monohydrate	17078303	2
Gehe	Lactose monohydrate	18198001	1
Gehe	Lactose monohydrate	1802002-01	1
Gehe	Lactose monohydrate	18198014	1
GEHE	Lactose monohydrate	17321001	1
GEHE	Lactose monohydrate	17321006	2
GEHE	Lactose monohydrate	17336005	1
GEHE	Lactose monohydrate	17336008	1
GEHE	Lactose monohydrate	17336014	2
GEHE	Lactose monohydrate	18198008	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
GEHE	Lactose monohydrate	18198017	1
GEHE am 17.06.2014	Lactose monohydrate	13299108	1
Caelo	Lactose monohydrate	17336001	1
Caelo	Lactose monohydrate	192364003	1
Kehr	Lactose monohydrate	17321004	1
L10	Lactose monohydrate	1606025-01	1
L12	Lactose monohydrate	1703019-01	1
L30	Lactose monohydrate	1703019-02	1
L30	Lactose monohydrate	1802002-01	1
Nachprüfung	Lactose monohydrate	3712Q-02210	1
Noweda	Lactose monohydrate	14025601	1
Noweda	Lactose monohydrate	1703019-01	1
Noweda	Lactose monohydrate	16231215	1
Noweda	Lactose monohydrate	17078303	1
Noweda/ Caesar&Loretz	Lactose monohydrate	12336815	1
Euro OTC	Lactose monohydrate	150903002	1
Euro OTC	Lactose monohydrate	150101701	1
otz pharma	Lactose monohydrate	130102802	1
Peter Kölln	Lactose monohydrate	229719241-0640	1
Peter Kölln GmbH & Co K...	Lactose monohydrate	256549266-0636	1
pharmachem	Lactose monohydrate	15236208	1
Phoenix	Lactose monohydrate	1404PLV-1928	4
Phoenix	Lactose monohydrate	15A19-B06	3
Phoenix	Lactose monohydrate	17321001	1
Phoenix	Lactose monohydrate	3194	1
Phoenix	Lactose monohydrate	17336013	1
Phoenix	Lactose monohydrate	1909014-01	1
Phoenix 19.03.2014	Lactose monohydrate	13104909	1
Phoenix 19.1.2019	Lactose monohydrate	18198001	1
Phoenix 30.04.2014	Lactose monohydrate	13E23-B01-283332	1
Phoenix 7.11.19	Lactose monohydrate	1802002-01	3
phönix	Lactose monohydrate	16231202	1
Phönix	Lactose monohydrate	12336815	1
Phönix	Lactose monohydrate	13299102	2
Phönix	Lactose monohydrate	14025616	1
Phönix	Lactose monohydrate	17321001	1
PHÖNIX	Lactose monohydrate	16A05-B03-322529	2
Phönix 17.05.2019	Lactose monohydrate	1812008-01	3
Phönix 28.08.2019	Lactose monohydrate	1812008-02	2
Caelo	Lactose monohydrate	18198023	2
Euro OTC	Lactose monohydrate	1509030-02	7
Euro OTC	Lactose monohydrate	180200201	2
Rondell Apotheke	Lactose monohydrate	1509030-01	2
Sanacorp	Lactose monohydrate	12336815	1
Sanacorp	Lactose monohydrate	13104901	1
Sanacorp	Lactose monohydrate	13104909	1
Sanacorp	Lactose monohydrate	13299102	1
Sanacorp	Lactose monohydrate	13299108	1
Sanacorp	Lactose monohydrate	14025620	1
Sanacorp	Lactose monohydrate	14333509	1
Sanacorp	Lactose monohydrate	14333518	1
Sanacorp	Lactose monohydrate	17078303	1
Sanacorp	Lactose monohydrate	17321004	1
Sanacorp,05.04.17, 5,96EUR	Lactose monohydrate	16231202	1
schubert / Phoenix	Lactose monohydrate	1334PLV-1775	1
siehe Protokoll	Lactose monohydrate	1606025-01	1
Spangropharm	Lactose monohydrate	91444379	1
vdl	Lactose monohydrate	1112020-01	2
Caelo	Lactose monohydrate	12139901	2
Caelo	Lactose monohydrate	12139915	4

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Supplier	Substance	Batch	Spectra
Caelo	Lactose monohydrate	309351/0	1
	Lactose monohydrate	309508/0	1
	Lactose monohydrate		1
	Lactose monohydrate	14025601	3
	Lactose monohydrate	12139910	1
	Lactose monohydrate	14025604	1

- 109 985 spectra from 742 *Apo-Ident* customers from a total of 31 505 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lactose monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lactose monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	430	0	110 259
Type B	0	200	0	118 942
Type C	0	1252	10	109 985

The substance/substance group *Lactose monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6047 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.2076 % (> 98.9699 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lactose monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pancreas powder	26.05	—
Aciclovir	38.64	—
Potassium tartrate hemihydrate	57.06	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lactose monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22460	22460	0.00	42.84
20685	22460	3.46	43.62
21525	22460	5.38	43.30
21526	22460	6.43	43.58
21527	22460	5.17	43.23
21528	22460	5.14	42.90
21529	22460	3.68	43.16
21935	21935	0.00	45.34
22701	22701	0.00	44.48
24929	24929	0.00	44.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Levocarnitine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20357-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Levocarnitine; Levocarnitivum

Special notes

When selecting the *Levocarnitine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Levocarnitine	5	3	9

Second-stage model

For differentiation of the substance/substance group *Levocarnitine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Levocarnitine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Levocarnitine	1210029-01	20809	40	20121130
Fagron	Levocarnitine	12H10-N07	20818	40	20120830
Fagron	Levocarnitine	14A20-B11-290728	21790	60	AR-15-FG-016322-01
Fagron	Levocarnitine	14A20-B11-290728	21968	60	AR-16-FG-005969-01
Fagron	Levocarnitine	15L04-B05-319229	23194	40	AR-17-FG-012937-01
Fagron	Levocarnitine	16L06-B03-338285	23919	40	20161227

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Levocarnitine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Levocarnitine*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Levocarnitine	1303027-02	21648	60
Fagron	Levocarnitine	16F20-B01-326616	23402	40
Fagron	Levocarnitine	17K23-B01-345633	24009	40

- 119 002 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 7 *Apo-Ident* customers from 9 batches from the substance/substance group *Levocarnitine*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Denk	Levocarnitine	A04217	1
Euro OTC	Levocarnitine	L1705006-01	1
Euro OTC	Levocarnitine	1705006-01	1
Euro OTC	Levocarnitine	L1801028-02	1
Euro OTC	Levocarnitine	L1608038-01	2
Euro OTC	Levocarnitine	1303027	1
Fagron	Levocarnitine	13G19-N12	2
Fagron	Levocarnitine	9041504	1
Fagron	Levocarnitine	13111701	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Levocarnitine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Levocarnitine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	140	0	119 002
Type C	0	11	0	111 236

The substance/substance group *Levocarnitine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Levocarnitine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	39.27	—
Choline hydrogen tartrate	54.25	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Levocarnitine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21968	21968	0.00	68.38
20809	23194	16.45	63.14
20818	23194	21.19	64.48
21790	21790	0.00	85.13
23194	23194	0.00	60.52
23919	23194	9.61	63.30

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Levothyroxin sodium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21708-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Levothyroxin sodium; Levothyroxinum natrii

Special notes

When selecting the *Levothyroxin sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Levothyroxin sodium	3	2	2

Second-stage model

For differentiation of the substance/substance group *Levothyroxin sodium* the following second-stage model is used:

- [Submodel 9](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Levothyroxin sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Levothyroxin sod...	14E28-B05-298322	21708	30	1506426
Fagron	Levothyroxin sod...	14E28-B05-298322	21708SI	47	1506426
Fagron	Levothyroxin sod...	14E28-B05-306102	21820	60	20140915
Fagron	Levothyroxin sod...	14E28-B05-306102	21820SI	53	20140915
Fagron	Levothyroxin sod...	18G27-B02-352032	24286	40	20180822

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 230 spectra of 5 reference samples from the substance/substance group *Levothyroxin sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 459 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 166 spectra of 5 reference samples from the substance/substance group *Levothyroxin sodium*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Levothyroxin sodium	16G25-B99-329080	23191	40
Fagron	Levothyroxin sodium	17J10-B05-348764	24176	40
Fagron	Levothyroxin sodium	16G25-B99-329080	23191SI	24
Fagron	Levothyroxin sodium	17J10-B05-348764	24176SI	30
Fagron	Levothyroxin sodium	18G27-B02-352032	24286SI [†]	32

- 118976 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 18 spectra from 5 *Apo-Ident* customers from 2 batches from the substance/substance group *Levothyroxin sodium*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Levothyroxin sodium	17J10-B05-345570	1
Fagron	Levothyroxin sodium	16G25-B99-324827	17

- 111 229 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Levothyroxin sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Levothyroxin sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	230	0	110 459
Type B	0	166	0	118 976
Type C	0	18	0	111 229

The substance/substance group *Levothyroxin sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.3913 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.3855 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Levothyroxin sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	45.52	—
Bismuth gallath, basic	62.73	—
⋮	⋮	⋮
Vancomycin hydrochloride	>50	98.99
Ethacridine lactate monohydrate	>50	300.40
Chlortetracycline hydrochloride	>50	350.25

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Levothyroxin sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21708	21708	0.00	65.98
21820	21708	17.73	75.10
24286	21708	20.99	77.45

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-glutathione**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20366-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-glutathione; L-Glutathionum

Special notes

When selecting the *L-glutathione* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-glutathione	4	3	2

Second-stage model

For differentiation of the substance/substance group *L-glutathione* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-glutathione*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	L-glutathione	1102019-02	21788	60	AR-15-FG-008218-01
Euro OTC	L-glutathione	1703008	23143	40	20170327*
Euro OTC	L-glutathione	1808036	24314	40	20180919*
Fagron	L-glutathione	18C01-B08-347604	24059	40	20180416

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *L-glutathione*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *L-glutathione*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-glutathione	1711009	23729	40
Euro OTC	L-glutathione	1901052	24491	40
Euro OTC	L-glutathione	1905011	24675	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *L-glutathione*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	L-glutathione	14H21-B02	1
Farmalabor	L-glutathione	P1700811	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-glutathione* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-glutathione* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	120	0	119 022
Type C	0	2	0	111 245

The substance/substance group *L-glutathione* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *L-glutathione* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carbomers 35000 / 50000	25.86	—
Magnesium citrate	39.90	—
Calcium citrate tetrahydrate	57.58	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-glutathione* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24314	24314	0.00	25.86
21788	21788	0.00	33.45
23143	23143	0.00	35.13
24059	23143	4.65	36.83

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Lidocaine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20942-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lidocaine; Lidocainum

Special notes

When selecting the *Lidocaine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lidocaine	7	8	208

Second-stage model

For differentiation of the substance/substance group *Lidocaine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lidocaine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Lidocaine	13352411	21673	60	20131115
Caelo	Lidocaine	180444	24031	40	20180419*
Euro OTC	Lidocaine	1310023-01	21640	60	20131118
Euro OTC	Lidocaine	1612021	22984	40	20170206*
Euro OTC	Lidocaine	1911005	24928	40	20191129*
Fagron	Lidocaine	13H05-N05	20942	40	1401378
Fagron	Lidocaine	16F21-B06-327232	23019	40	20160728

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Lidocaine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 369 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 8 reference samples from the substance/substance group *Lidocaine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Lidocaine	162895	22768	40
Caelo	Lidocaine	171831	23632	40
Caelo	Lidocaine	190545	24530	40
Euro OTC	Lidocaine	1603027	22526	40
Euro OTC	Lidocaine	1801032	23960	40
Euro OTC	Lidocaine	1902003	24475	40
Euro OTC	Lidocaine	1905004	24610	40
Euro OTC	Lidocaine	1908005	24847	40

- 118 822 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 645 spectra from 292 *Apo-Ident* customers from 221 batches from the substance/substance group *Lidocaine*.
- Among them are spectra of independent samples from 210 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Lidocaine	16F21-806-333787	1
Fagron	Lidocaine	17K23-B04-350542	1
AHD	Lidocaine	15332314	1
Alliance	Lidocaine	15H27-B07-318310	1
Allianz Healthcare	Lidocaine	8565960	1
Alte Apotheke	Lidocaine	16A28B06-321297	1
Anzag	Lidocaine	12E30-N10	1
Fagron	Lidocaine	16F21B06332251	1
Caelo	Lidocaine	12294408	2
Caelo	Lidocaine	15332306	3
Caelo	Lidocaine	5111201	1
Caelo	Lidocaine	12163803	3
Caelo	Lidocaine	12163804	2
Caelo	Lidocaine	12163802	2
Caelo	Lidocaine	9205919	1
Caelo	Lidocaine	12163811	3
Caelo	Lidocaine	12163810	1
Caelo	Lidocaine	12163813	5
Caelo	Lidocaine	12294412	10
Caelo	Lidocaine	12294405	2
Caelo	Lidocaine	122294405	1
Caelo	Lidocaine	13352403	1
Caelo	Lidocaine	14299301	2
Caelo	Lidocaine	16087704	8
Caelo	Lidocaine	133524	1

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Supplier	Substance	Batch	Spectra
Caelo	Lidocaine	13352413	3
Caelo	Lidocaine	14299303	2
Caelo	Lidocaine	13352415	3
Caelo	Lidocaine	15212003	3
Caelo	Lidocaine	15A15-B01-304284	3
Caelo	Lidocaine	15332302	4
Caelo	Lidocaine	1512003	1
Caelo	Lidocaine	8629595	1
Caelo	Lidocaine	15332309	2
Caelo	Lidocaine	16087703	1
Caelo	Lidocaine	15332310	4
Caelo	Lidocaine	16087702	1
Caelo	Lidocaine	16087707	7
Caelo	Lidocaine	16087710	2
Caelo	Lidocaine	16087709	1
Caelo	Lidocaine	9205916	2
Caelo	Lidocaine	16289503	6
Caelo	Lidocaine	160877708	1
Caelo	Lidocaine	16087708	1
Caelo	Lidocaine	16289504	2
Caelo	Lidocaine	16289508	14
Caelo	Lidocaine	17183105	1
Caelo	Lidocaine	17183103	3
Caelo	Lidocaine	17348502	5
Caelo	Lidocaine	18041812	1
Caelo	Lidocaine	17G03-B08	1
Caelo	Lidocaine	17348503	9
Caelo	Lidocaine	17183106	1
Caelo	Lidocaine	1612021-04	1
Caelo	Lidocaine	17K23-B04-350543	1
Caelo	Lidocaine	18044405	1
Caelo	Lidocaine	17K23-B04-347475	1
Caelo	Lidocaine	17K23-B04-353247	1
Caelo	Lidocaine	19054506	1
Caelo	Lidocaine	13352406	1
Caelo	Lidocaine	15332314	2
Caelo	Lidocaine	17G03-B08-341306	2
Caelo	Lidocaine	17K23-B04-343250	1
Caelo	Lidocaine	17K23-B04-347473	1
Caelo	Lidocaine	18044402	3
Caelo	Lidocaine	18044408	5
Caelo	Lidocaine	15212002	3
Caelo	Lidocaine	15212001	2
Caelo	Lidocaine	1804413	1
Caelo	Lidocaine	15332305	2
Caelo	Lidocaine	19054503	1
Caelo	Lidocaine	18044404	6
Caelo	Lidocaine	15H-B07-318310	1
Caelo	Lidocaine	19054505	1
Caelo	Lidocaine	19f27-b01-363506	1
Caelo	Lidocaine	15H27-B07-318310	1
Caelo	Lidocaine	18044413	5
Caelo	Lidocaine	18044415	2
Caelo	Lidocaine	14299305	2
Caelo	Lidocaine	11K17-N03	1
Caelo	Lidocaine	13352408	8
Caelo	Lidocaine	13352414	2
Caelo	Lidocaine	15332303	1
Caelo	Lidocaine	16087712	7
Caelo	Lidocaine	17183102	2

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Supplier	Substance	Batch	Spectra
Caelo	Lidocaine	1718308	1
Caelo	Lidocaine	17G03B08341308	1
Caelo	Lidocaine	1804404	1
Caelo	Lidocaine	16A28-B06-320059	1
Caelo	Lidocaine	1629508	1
Caelo	Lidocaine	180444404	1
Caelo	Lidocaine	16087711	10
Caelo	Lidocaine	16F21-B06-323670	1
Caelo	Lidocaine	16F21-B06-328421	3
Caelo	Lidocaine	17183108	8
Caelo	Lidocaine	17183109	4
Caelo	Lidocaine	18044410	2
Caelo	Lidocaine	13352405	1
Caelo	Lidocaine	15D23-B08	1
Caelo	Lidocaine	16289502	8
Caelo	Lidocaine	1783109	2
Caelo	Lidocaine	1804410	1
Caesar & Loretz GmbH	Lidocaine	12294412	1
Caesar & Loretz GmbH	Lidocaine	18044414	1
Caesar & Loretz GmbH	Lidocaine	18044410	1
Caesar & Loretz GmbH / ...	Lidocaine	18044405	1
Caesar & Loretz GmbH /E	Lidocaine	18044413	1
Caesar & Loretz GmbH/Ph...	Lidocaine	18044410	1
Caesar&Loretz GmbH	Lidocaine	16289502	1
Caesar&Loretz,Phönix,06...	Lidocaine	15332314	1
Cealo	Lidocaine	17348503	1
Ebert-Jacobi	Lidocaine	16289504	1
Euro OTC	Lidocaine	1310023-02	3
Euro OTC	Lidocaine	17348503	1
Euro OTC	Lidocaine	1902003-01	3
Euro OTC	Lidocaine	1612021-01	2
Euro OTC	Lidocaine	1612021-02	5
Euro OTC	Lidocaine	1612021-04	4
Euro OTC	Lidocaine	1908005-01	2
Euro OTC	Lidocaine	1603027-02	1
Euro OTC	Lidocaine	161202102	2
Euro OTC	Lidocaine	17K23B04345215	1
Euro OTC	Lidocaine	1603027-01	2
Fagron/Gehe	Lidocaine	15a15b01304284	1
Fagron	Lidocaine	12h16-N05	1
Fagron	Lidocaine	12I21N06	1
Fagron	Lidocaine	12C08-N11	2
Fagron	Lidocaine	11D28-N12	1
Fagron	Lidocaine	11K17-N03	1
Fagron	Lidocaine	6J23-No2	1
Fagron	Lidocaine	12H16-N05	5
Fagron	Lidocaine	12I21-N06	3
Fagron	Lidocaine	12H16-n05	1
Fagron	Lidocaine	12K13-N01	1
Fagron	Lidocaine	12/21-N06	3
Fagron	Lidocaine	11C09-N07	2
Fagron	Lidocaine	13H05-N050171/245	1
Fagron	Lidocaine	13J30-B02-292221	5
Fagron	Lidocaine	13J30-B02	6
Fagron	Lidocaine	13J30-B02-287641	6
Fagron	Lidocaine	13J30-B02-292220	2
Fagron	Lidocaine	14E13-B05-295549	4
Fagron	Lidocaine	5122014A	1
Fagron	Lidocaine	14E13-B05-295550	2
Fagron	Lidocaine	15A15-B01-304283	2

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Supplier	Substance	Batch	Spectra
Fagron	Lidocaine	15D23-B08-309882	1
Fagron	Lidocaine	15D23-B08-31058	1
Fagron	Lidocaine	15D23-B08_312058	1
Fagron	Lidocaine	15D23B08311708	1
Fagron	Lidocaine	15d23-b08-312058	2
Fagron	Lidocaine	15h27-b05-318310	1
Fagron	Lidocaine	15H27-B07-318310	3
Fagron	Lidocaine	16A28B06320059	1
Fagron	Lidocaine	5742	1
Fagron	Lidocaine	16F21-B06-328421	7
Fagron	Lidocaine	16289508	1
Fagron	Lidocaine	16F21	2
Fagron	Lidocaine	16F21-B06-333787	1
Fagron	Lidocaine	16f21-b06-335659	1
Fagron	Lidocaine	17G03-B08-338286	3
Fagron	Lidocaine	17G03-B08	4
Fagron	Lidocaine	17G03-B08-341308	3
Fagron	Lidocaine	17K23-B04-345215	6
Fagron	Lidocaine	17k23-b04-347475	1
Fagron	Lidocaine	17K23-B04-350541	4
Fagron	Lidocaine	17K23B04353428	1
Fagron	Lidocaine	17K23-B04-353428	2
Fagron	Lidocaine	17K23-B04-353247	4
Fagron	Lidocaine	LDB/117093	2
Fagron	Lidocaine	17K23-B04-355709	3
Fagron	Lidocaine	18J23-B02-359239	3
Fagron	Lidocaine	17K23B04350189	1
Fagron	Lidocaine	18J23B02359239	1
Fagron	Lidocaine	18j23-B02-359237	1
Fagron	Lidocaine	17K23-B04-345948	2
Fagron	Lidocaine	17G03-B08-341306	4
Fagron	Lidocaine	16F21-B06-333788	1
Fagron	Lidocaine	13B27-N04	8
Fagron	Lidocaine	LDB/116049	1
Fagron	Lidocaine	18J23-B02356573	1
Fagron	Lidocaine	15H27-B07-316784	1
Fagron	Lidocaine	700412-0004	1
Fagron	Lidocaine	17G03-B08-343251	1
Fagron	Lidocaine	13J30-B02-292219	2
Fagron	Lidocaine	17K23-B04-353427	2
Fagron	Lidocaine	15H27-B07	1
Fagron	Lidocaine	12h16_n05	1
Fagron	Lidocaine	13E28-B40-289433	1
Fagron	Lidocaine	15D23-B08_309882	1
Fagron	Lidocaine	17K23-B04-343250	2
Fagron	Lidocaine	18J23-B02-359237	2
Fagron	Lidocaine	17K23-B04-350543	4
Fagron	Lidocaine	18J23-B02-3557018	1
Fagron	Lidocaine	16F21-B06-323670	14
Fagron	Lidocaine	16F21-B06-332253	1
Fagron	Lidocaine	17K23-B04-350189	4
Fagron	Lidocaine	17K23-B04	6
Fagron	Lidocaine	15A15-B01-304282	4
Fagron	Lidocaine	15d23-b08-309882	1
Fagron	Lidocaine	16F21-B06	2
Fagron	Lidocaine	14E13-B05	2
Fagron	Lidocaine	13J30-b02-287639	1
Fagron	Lidocaine	214U-03584	1
Fagron	Lidocaine	15A15B01304284	1
Fagron	Lidocaine	15D23-B08-312058	11

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Supplier	Substance	Batch	Spectra
Fagron	Lidocaine	16F21-B06-325934	2
Fagron	Lidocaine	1330-B02-287641	1
Fagron	Lidocaine	17K23-B04-347473	3
Fagron	Lidocaine	14E13-B05-295552	3
Fagron	Lidocaine	1113M-03584	1
Fagron	Lidocaine	1014I-07006	1
Fagron	Lidocaine	515M-07006	1
Fagron	Lidocaine	1116E-07006	1
Fagron	Lidocaine	13j30B02292219	1
Fagron	Lidocaine	15A15-B01-304284	7
Fagron	Lidocaine	15A15-B01	1
Fagron	Lidocaine	16F21-B06-328421	1
Fagron	Lidocaine	16F21-B06-335659	1
Fagron	Lidocaine	17K23-B04-347475	8
Fagron	Lidocaine	1612021-01	1
Fagron	Lidocaine	18j23bo2359239	1
Fagron	Lidocaine	15D23-B08	1
Fagron	Lidocaine	16F21-B06-323669	5
Fagron	Lidocaine	16F21B06325934	1
Fagron	Lidocaine	17K23-B04-347474	4
Fagron	Lidocaine	18J23-B02-359238	3
Fagron	Lidocaine	19F27-B01-363502	5
Fagron	Lidocaine	19F27-B01-363500	3
Fagron	Lidocaine	17K23B04347473	1
Fagron	Lidocaine	13J30-B02-287640	1
Fagron	Lidocaine	15H27-B07-315483	2
Fagron	Lidocaine	16A28-B06-320059	2
Fagron	Lidocaine	16F21-B06-332253	5
Fargon	Lidocaine	12E30-N10	1
Fargon/Phoenix	Lidocaine	13H05-N05	3
Fargron	Lidocaine	14E13-B05-295552	1
Faron/Alliance	Lidocaine	16F21-B06-323670	2
Gatt-Koller	Lidocaine	1900471	1
Gehe	Lidocaine	13B27-N04	1
Gehe	Lidocaine	12H16-N05	1
Gehe	Lidocaine	14E13-B05-295552	1
Gehe	Lidocaine	18J23-B02-359239	1
Gehe	Lidocaine	19054505	2
GEHE	Lidocaine	16289503	1
GEHE	Lidocaine	16F21-B06-328421	1
GEHE	Lidocaine	18044405	1
GEHE 02.12.2014	Lidocaine	13J30-B02-292220	1
Gehe am 22.01.2014	Lidocaine	13H05-N05	2
Gehe Kassel	Lidocaine	14E13-B05-295550	1
Fagron	Lidocaine	71-18	1
Fagron	Lidocaine	12E30-N10	8
Gutenberg-Apotheke	Lidocaine	13J30-B02	1
Kehr	Lidocaine	16F21-B06-328421	1
Kehr	Lidocaine	16F21-B06-332251	1
Kehr	Lidocaine	17G03-B08-338284	1
LaVita	Lidocaine	15H27-B07-318310	1
Moehs BCN S.L. / Noweda	Lidocaine	15332305	1
Nachprüfung von Juni 2018	Lidocaine	12C08-N11	1
Noweda	Lidocaine	12H16-N05	1
Noweda	Lidocaine	17K23-B04-350542	1
Noweda	Lidocaine	18J23-B02-355708	3
Pharmachem	Lidocaine	17K23-B04-350541	1
phoenix	Lidocaine	17348503	1
Phoenix	Lidocaine	15332305	1
Phoenix	Lidocaine	17K23-B05-345948	1

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Supplier	Substance	Batch	Spectra
Phoenix	Lidocaine	18J23-B02-359238	1
Phoenix	Lidocaine	1905004-01	1
Phoenix	Lidocaine	19054504	1
PHOENIX 22.08.2014	Lidocaine	13J30-B02-287640	1
Phönix	Lidocaine	13B27-N04	1
Phönix	Lidocaine	17K23-B04-347475	1
Phönix	Lidocaine	17K23-B04-343250	1
Phönix	Lidocaine	19F27-B01-363505	1
Phönix Gotha	Lidocaine	15A15-B01-304284	1
Caelo	Lidocaine	16289507	2
Rondell Apotheke	Lidocaine	15332304	1
Sanacorp	Lidocaine	12H16-N05	1
Sanacorp	Lidocaine	12I21-N06	1
Sanacorp	Lidocaine	1603027-02	1
Sanacorp	Lidocaine	17183109	1
Caelo	Lidocaine	13J30-B02-292221	1
Fagron	Lidocaine	17G23-B04-350541	1
Fagron	Lidocaine	13H05-N05	8
Caelo	Lidocaine	13352411	6
Fagron	Lidocaine		1
Fagron	Lidocaine	16F21-B06-327232	2
Henry Lamotte Oils GmbH	Lidocaine		1
PHOENIX 22.08.2014	Lidocaine		2

- 110 602 spectra from 742 *Apo-Ident* customers from a total of 31 672 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lidocaine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lidocaine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	320	0	118 822
Type C	0	644	1	110 602

The substance/substance group *Lidocaine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 99.8899 %)	99.8450 % (> 99.3798 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lidocaine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol hemihydrate	42.31	—
Dexamethasone	42.76	—
Ethosuximide	47.51	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lidocaine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20942	20942	0.00	42.56
21640	22984	6.50	42.87
21673	24031	7.13	42.31
22984	22984	0.00	43.24
23019	22984	3.04	42.66
24031	24031	0.00	43.16
24928	24928	0.00	45.67

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Lidocaine hydrochloride monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20093-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lidocaine hydrochloride monohydrate; Lidocaini hydrochloridum monohydricum

Special notes

When selecting the *Lidocaine hydrochloride monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lidocaine hydrochloride monohydrate	5	6	277

Second-stage model

For differentiation of the substance/substance group *Lidocaine hydrochloride monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lidocaine hydrochloride monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Lidocaine hydroc...	12135511	20882	40	AR-15-FG-008867-01
Caelo	Lidocaine hydroc...	172923	23807	40	20171122*
Euro OTC	Lidocaine hydroc...	1403025-02	21613	60	20140516
Euro OTC	Lidocaine hydroc...	1411010	21770	60	20150126*
Euro OTC	Lidocaine hydroc...	1907012	24776	40	20190801*

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Lidocaine hydrochloride monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Lidocaine hydrochloride monohydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Lidocaine hydrochloride mono...	162222	22771	40
Caelo	Lidocaine hydrochloride mono...	152995	22772	40
Caelo	Lidocaine hydrochloride mono...	172048	23687	40
Euro OTC	Lidocaine hydrochloride mono...	1606024	22702	40
Euro OTC	Lidocaine hydrochloride mono...	1612015	22980	40
Euro OTC	Lidocaine hydrochloride mono...	1808031	24326	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1454 spectra from 503 *Apo-Ident* customers from 289 batches from the substance/substance group *Lidocaine hydrochloride monohydrate*.
- Among them are spectra of independent samples from 279 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
01.07.14	Lidocaine hydrochloride mono...	13343004	1
A.H.D.	Lidocaine hydrochloride mono...	1202035-02	1
ACM	Lidocaine hydrochloride mono...	KNC1247J15	1
ACM	Lidocaine hydrochloride mono...	KNC0625J17	1
AHD	Lidocaine hydrochloride mono...	17292308	2
AHD	Lidocaine hydrochloride mono...	17292313	1
AHD	Lidocaine hydrochloride mono...	18179904	1
AHD	Lidocaine hydrochloride mono...	17292311	1
AHD	Lidocaine hydrochloride mono...	18179910	1
Fagron	Lidocaine hydrochloride mono...	13218-B11	1
ALH	Lidocaine hydrochloride mono...	1606024-01	1
ALH/EuRho	Lidocaine hydrochloride mono...	1612015-01	1
Euro OTC	Lidocaine hydrochloride mono...	18080031	1
Alliance health	Lidocaine hydrochloride mono...	14B12-B03-292214	1
Caelo	Lidocaine hydrochloride mono...	13343002	3
Allianz	Lidocaine hydrochloride mono...	17292308	1
Alte Apotheke	Lidocaine hydrochloride mono...	1606024-01	2
Anzag	Lidocaine hydrochloride mono...	1202035-03	1
Anzag	Lidocaine hydrochloride mono...	1403025-01	1
Anzag	Lidocaine hydrochloride mono...	14B12-B03-292214	1
Anzag	Lidocaine hydrochloride mono...	1411010-01	1
Anzag	Lidocaine hydrochloride mono...	17204804	2
Fagron	Lidocaine hydrochloride mono...	12H09-N08	2
Euro OTC	Lidocaine hydrochloride mono...	1612015	4
Fagron	Lidocaine hydrochloride mono...	LDH/117022	1
Apo-Ident, Phönix, 7.11...	Lidocaine hydrochloride mono...	1612015-01	1
Bombastus	Lidocaine hydrochloride mono...	1612015-02	1
Bombastus	Lidocaine hydrochloride mono...	15215301	1
Bombastus	Lidocaine hydrochloride mono...	180831-01	1
Caelo	Lidocaine hydrochloride mono...	13343001	2
Caelo	Lidocaine hydrochloride mono...	16101407	1
Caelo	Lidocaine hydrochloride mono...	17292307	2

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Supplier	Substance	Batch	Spectra
Caelo	Lidocaine hydrochloride mono...	1612015-03	1
Caelo	Lidocaine hydrochloride mono...	18179906	3
Caelo	Lidocaine hydrochloride mono...	10320703	1
Caelo	Lidocaine hydrochloride mono...	11091203	1
Caelo	Lidocaine hydrochloride mono...	10320704	1
Caelo	Lidocaine hydrochloride mono...	25091202	1
Caelo	Lidocaine hydrochloride mono...	12176101	8
Caelo	Lidocaine hydrochloride mono...	5211E-01775	1
Caelo	Lidocaine hydrochloride mono...	11302904	1
Caelo	Lidocaine hydrochloride mono...	12135504	3
Caelo	Lidocaine hydrochloride mono...	12176103	8
Caelo	Lidocaine hydrochloride mono...	11302902	2
Caelo	Lidocaine hydrochloride mono...	11302905	1
Caelo	Lidocaine hydrochloride mono...	2051301	1
Caelo	Lidocaine hydrochloride mono...	12135509	4
Caelo	Lidocaine hydrochloride mono...	10320719	1
Caelo	Lidocaine hydrochloride mono...	26071303	1
Caelo	Lidocaine hydrochloride mono...	4111302	1
Caelo	Lidocaine hydrochloride mono...	1202035-03	1
Caelo	Lidocaine hydrochloride mono...	23011403	1
Caelo	Lidocaine hydrochloride mono...	1202035	1
Caelo	Lidocaine hydrochloride mono...	13118812	3
Caelo	Lidocaine hydrochloride mono...	26041401	1
Caelo	Lidocaine hydrochloride mono...	13343008	5
Caelo	Lidocaine hydrochloride mono...	24071401	1
Caelo	Lidocaine hydrochloride mono...	13343012	16
Caelo	Lidocaine hydrochloride mono...	13343014	5
Caelo	Lidocaine hydrochloride mono...	12021503	1
Caelo	Lidocaine hydrochloride mono...	18041501	1
Caelo	Lidocaine hydrochloride mono...	1411010-01	2
Caelo	Lidocaine hydrochloride mono...	13343019	4
Caelo	Lidocaine hydrochloride mono...	29081503	1
Caelo	Lidocaine hydrochloride mono...	15215311	4
Caelo	Lidocaine hydrochloride mono...	15215312	7
Caelo	Lidocaine hydrochloride mono...	160719LC	1
Caelo	Lidocaine hydrochloride mono...	15299513	8
Caelo	Lidocaine hydrochloride mono...	16222202	2
Caelo	Lidocaine hydrochloride mono...	1606024	1
Caelo	Lidocaine hydrochloride mono...	160602401	1
Caelo	Lidocaine hydrochloride mono...	16222214	13
Caelo	Lidocaine hydrochloride mono...	812-16001	1
Caelo	Lidocaine hydrochloride mono...	1606024-03	3
Caelo	Lidocaine hydrochloride mono...	17204804	25
Caelo	Lidocaine hydrochloride mono...	4111703	1
Caelo	Lidocaine hydrochloride mono...	6121706	1
Caelo	Lidocaine hydrochloride mono...	160602403	1
Caelo	Lidocaine hydrochloride mono...	26051802	1
Caelo	Lidocaine hydrochloride mono...	17292310	1
Caelo	Lidocaine hydrochloride mono...	17292313	4
Caelo	Lidocaine hydrochloride mono...	1808031-01	8
Caelo	Lidocaine hydrochloride mono...	28111812	1
Caelo	Lidocaine hydrochloride mono...	1729308	1
Caelo	Lidocaine hydrochloride mono...	2021903	1
Caelo	Lidocaine hydrochloride mono...	18179911	4
Caelo	Lidocaine hydrochloride mono...	18179910	2
Caelo	Lidocaine hydrochloride mono...	18B23-B03-355046	1
Caelo	Lidocaine hydrochloride mono...	18179914	1
Caelo	Lidocaine hydrochloride mono...	15215301	7
Caelo	Lidocaine hydrochloride mono...	4051703	1
Caelo	Lidocaine hydrochloride mono...	3071711	1

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Supplier	Substance	Batch	Spectra
Caelo	Lidocaine hydrochloride mono...	13118802	2
Caelo	Lidocaine hydrochloride mono...	10320707	2
Caelo	Lidocaine hydrochloride mono...	12135503	2
Caelo	Lidocaine hydrochloride mono...	12176102	8
Caelo	Lidocaine hydrochloride mono...	12135508	5
Caelo	Lidocaine hydrochloride mono...	1612015-04	2
Caelo	Lidocaine hydrochloride mono...	14J20-B05-303131	1
Caelo	Lidocaine hydrochloride mono...	1403025-02	2
Caelo	Lidocaine hydrochloride mono...	18179924	1
Caelo	Lidocaine hydrochloride mono...	1606024-01	17
Caelo	Lidocaine hydrochloride mono...	1505023-02	1
Caelo	Lidocaine hydrochloride mono...	1729313	1
Caelo	Lidocaine hydrochloride mono...	13118803	5
Caelo	Lidocaine hydrochloride mono...	13343015	2
Caelo	Lidocaine hydrochloride mono...	5113E-01775	1
Caelo	Lidocaine hydrochloride mono...	10320717	1
Caelo	Lidocaine hydrochloride mono...	17204810	2
Caelo	Lidocaine hydrochloride mono...	1612015-01	4
Caelo	Lidocaine hydrochloride mono...	13(1808031-01)	1
Caelo	Lidocaine hydrochloride mono...	17292311	2
Caelo	Lidocaine hydrochloride mono...	15299509	3
Caelo	Lidocaine hydrochloride mono...	15215309	2
Caelo	Lidocaine hydrochloride mono...	1729311	1
Caelo	Lidocaine hydrochloride mono...	17292316	2
Caelo	Lidocaine hydrochloride mono...	1411010-02	1
Caelo	Lidocaine hydrochloride mono...	15117-B01	1
Caelo	Lidocaine hydrochloride mono...	15215302	2
Caelo	Lidocaine hydrochloride mono...	17292308	3
Caelo	Lidocaine hydrochloride mono...	1792313	1
Caelo	Lidocaine hydrochloride mono...	18179915	1
Caelo	Lidocaine hydrochloride mono...	15215201	3
Caelo	Lidocaine hydrochloride mono...	15299514	7
Caelo	Lidocaine hydrochloride mono...	1912M-01775	1
Caelo	Lidocaine hydrochloride mono...	1814U-01775	1
Caelo	Lidocaine hydrochloride mono...	1515I-01775	1
Caelo	Lidocaine hydrochloride mono...	17292302	5
Caelo	Lidocaine hydrochloride mono...	120203501	1
Caelo	Lidocaine hydrochloride mono...	12176109	2
Caelo	Lidocaine hydrochloride mono...	13343004	7
Caelo	Lidocaine hydrochloride mono...	15299503	9
Caelo	Lidocaine hydrochloride mono...	1230817/160602402	1
Caelo	Lidocaine hydrochloride mono...	1612015_02	1
Caelo	Lidocaine hydrochloride mono...	18179904	8
Caelo	Lidocaine hydrochloride mono...	16222208	5
Caelo	Lidocaine hydrochloride mono...	17292304	21
Caelo	Lidocaine hydrochloride mono...	13343017	5
Caelo	Lidocaine hydrochloride mono...	1808031-02	1
Caelo	Lidocaine hydrochloride mono...	15215303	2
Caelo	Lidocaine hydrochloride mono...	16222207	5
Caelo	Lidocaine hydrochloride mono...	13343011	3
Caelo	Lidocaine hydrochloride mono...	14110101	1
Caelo	Lidocaine hydrochloride mono...	1505023-01	6
Caelo	Lidocaine hydrochloride mono...	15299516	7
Caelo	Lidocaine hydrochloride mono...	152951602714117	1
Caelo	Lidocaine hydrochloride mono...	16222203	7
Caelo	Lidocaine hydrochloride mono...	17204803	10
Caelo	Lidocaine hydrochloride mono...	17292301	1
Caelo	Lidocaine hydrochloride mono...	280501	1
Caelo	Lidocaine hydrochloride mono...	1612015-05	1
Caelo	Lidocaine hydrochloride mono...	1808031-03	1

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Supplier	Substance	Batch	Spectra
Caelo	Lidocaine hydrochloride mono...	15215310	9
Caelo	Lidocaine hydrochloride mono...	16120515-02	1
Caelo	Lidocaine hydrochloride mono...	1202035-02	5
Caelo	Lidocaine hydrochloride mono...	1505023-03	2
Caelo	Lidocaine hydrochloride mono...	1606024-02	5
Caelo	Lidocaine hydrochloride mono...	LDH/118024	1
Caelo	Lidocaine hydrochloride mono...	19135103	4
Caelo	Lidocaine hydrochloride mono...	13118808	4
Caelo	Lidocaine hydrochloride mono...	13118811	2
Caelo	Lidocaine hydrochloride mono...	13343003	5
Caelo	Lidocaine hydrochloride mono...	14254001	3
Caelo	Lidocaine hydrochloride mono...	15215304	3
Caelo	Lidocaine hydrochloride mono...	1521304	1
Caelo	Lidocaine hydrochloride mono...	15299506	3
Caelo	Lidocaine hydrochloride mono...	1612015-02	7
Caelo	Lidocaine hydrochloride mono...	18179923	1
Caelo	Lidocaine hydrochloride mono...	16083001	1
Caelo	Lidocaine hydrochloride mono...	15215308	2
Caelo	Lidocaine hydrochloride mono...	13343016	1
Caerlo	Lidocaine hydrochloride mono...	13118807	1
Caesar & Lorenz GmbH	Lidocaine hydrochloride mono...	16222208	1
Caesar & Loretz	Lidocaine hydrochloride mono...	1612015-01	2
Caesar & Loretz GmbH	Lidocaine hydrochloride mono...	13343002	1
Caesar & Loretz GmbH	Lidocaine hydrochloride mono...	15215201	1
Caesar & Loretz GmbH	Lidocaine hydrochloride mono...	18179904	3
Caesar & Loretz GmbH	Lidocaine hydrochloride mono...	18179911	2
Caesar & Loretz GmbH/Ge...	Lidocaine hydrochloride mono...	18179914	1
Caesar & Loretz GmbH/Gö...	Lidocaine hydrochloride mono...	19135103	1
Caesar & Loretz/Anzag d...	Lidocaine hydrochloride mono...	18179906	1
Caesar u Loretz	Lidocaine hydrochloride mono...	13343017	1
Caesar&Loretz GmbH /Anzag	Lidocaine hydrochloride mono...	15215303	1
Caesar&Loretz GmbH/ San...	Lidocaine hydrochloride mono...	17204803	1
Caesar&Loretz GmbH/Anzag	Lidocaine hydrochloride mono...	13118803	2
Caesar und Loretz GmbH	Lidocaine hydrochloride mono...	181799023	1
Caolo	Lidocaine hydrochloride mono...	13343008	1
Ensbona/ Sanacorp	Lidocaine hydrochloride mono...	1606024-01	1
EuRho	Lidocaine hydrochloride mono...	1108017-01	2
EuRho	Lidocaine hydrochloride mono...	140302501	1
EuRho	Lidocaine hydrochloride mono...	1505023-01	3
EuRho	Lidocaine hydrochloride mono...	1505023-02	1
EuRho	Lidocaine hydrochloride mono...	1612015-01	2
EuRho	Lidocaine hydrochloride mono...	161201502	1
EuRho/Phoenix	Lidocaine hydrochloride mono...	1612015-01	1
Euro	Lidocaine hydrochloride mono...	1505023-01	2
Euro OTC	Lidocaine hydrochloride mono...	1411010-02	23
Euro OTC	Lidocaine hydrochloride mono...	150502301	2
Euro OTC	Lidocaine hydrochloride mono...	160602402	1
Euro OTC	Lidocaine hydrochloride mono...	16112015-01	2
Euro OTC	Lidocaine hydrochloride mono...	23081601	1
Euro OTC	Lidocaine hydrochloride mono...	1108017-02	7
Euro OTC	Lidocaine hydrochloride mono...	1202034-01	2
Euro OTC	Lidocaine hydrochloride mono...	20131010-4	1
Euro OTC	Lidocaine hydrochloride mono...	2213U01775	1
Euro OTC	Lidocaine hydrochloride mono...	2810029-01	1
Euro OTC	Lidocaine hydrochloride mono...	1202035-03	11
Euro OTC	Lidocaine hydrochloride mono...	120203502	3
Euro OTC	Lidocaine hydrochloride mono...	140302501	2
Euro OTC	Lidocaine hydrochloride mono...	140302502	2
Euro OTC	Lidocaine hydrochloride mono...	141101002	3
Euro OTC	Lidocaine hydrochloride mono...	1505023-03	16

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Supplier	Substance	Batch	Spectra
Euro OTC	Lidocaine hydrochloride mono...	160602401	3
Euro OTC	Lidocaine hydrochloride mono...	2886	1
Euro OTC	Lidocaine hydrochloride mono...	16006024-02	1
Euro OTC	Lidocaine hydrochloride mono...	1606024-03	12
Euro OTC	Lidocaine hydrochloride mono...	ldh/116023	1
Euro OTC	Lidocaine hydrochloride mono...	161201502	3
Euro OTC	Lidocaine hydrochloride mono...	1612012015-04	1
Euro OTC	Lidocaine hydrochloride mono...	1411010-02Mg50g	1
Euro OTC	Lidocaine hydrochloride mono...	16112015-04	1
Euro OTC	Lidocaine hydrochloride mono...	171106LHC/1606024-03	1
Euro OTC	Lidocaine hydrochloride mono...	1907012-01	12
Euro OTC	Lidocaine hydrochloride mono...	1202035-01	24
Euro OTC	Lidocaine hydrochloride mono...	1612015_01	1
Euro OTC	Lidocaine hydrochloride mono...	1907012_01	1
Euro OTC	Lidocaine hydrochloride mono...	1108017-01	5
Euro OTC	Lidocaine hydrochloride mono...	1202035-1	1
Euro OTC	Lidocaine hydrochloride mono...	1403025-01	20
Euro OTC	Lidocaine hydrochloride mono...	1411010-01	33
Euro OTC	Lidocaine hydrochloride mono...	140415A	1
Euro OTC	Lidocaine hydrochloride mono...	1401010-01	1
Euro OTC	Lidocaine hydrochloride mono...	141101	1
Euro OTC	Lidocaine hydrochloride mono...	1606021-01	1
Euro OTC	Lidocaine hydrochloride mono...	17204810	1
Euro OTC	Lidocaine hydrochloride mono...	1612015-04	20
Euro OTC	Lidocaine hydrochloride mono...	1403025-03	1
Euro OTC	Lidocaine hydrochloride mono...	160624-01	1
Euro OTC	Lidocaine hydrochloride mono...	1618015-02	1
Euro OTC	Lidocaine hydrochloride mono...	1612015-03	15
Euro OTC	Lidocaine hydrochloride mono...	161201504	3
Euro OTC	Lidocaine hydrochloride mono...	1612015-05	1
Euro OTC	Lidocaine hydrochloride mono...	1808031-04	1
Euro OTC	Lidocaine hydrochloride mono...	18908031-01	1
Euro OTC	Lidocaine hydrochloride mono...	1808031-03	4
Euro OTC	Lidocaine hydrochloride mono...	17204803	2
Euro OTC	Lidocaine hydrochloride mono...	1808031-02	21
Euro OTC	Lidocaine hydrochloride mono...	1004040-01	1
Euro OTC	Lidocaine hydrochloride mono...	14110101-01	1
Euro OTC	Lidocaine hydrochloride mono...	1411010-2	1
Euro OTC	Lidocaine hydrochloride mono...	1202035/02	1
Euro OTC	Lidocaine hydrochloride mono...	1411010-01Mg25g	1
Euro OTC	Lidocaine hydrochloride mono...	1606024-01	56
Euro OTC	Lidocaine hydrochloride mono...	LID-20-11-001	2
Euro OTC	Lidocaine hydrochloride mono...	1808031	4
Euro OTC	Lidocaine hydrochloride mono...	1140917/160602403	1
Euro OTC	Lidocaine hydrochloride mono...	1103034-01	2
Euro OTC	Lidocaine hydrochloride mono...	141101-01	1
Euro OTC	Lidocaine hydrochloride mono...	1403025	1
Euro OTC	Lidocaine hydrochloride mono...	150523-02	1
Euro OTC	Lidocaine hydrochloride mono...	170612182	1
Euro OTC	Lidocaine hydrochloride mono...	180220L/1612015-01	1
Euro OTC	Lidocaine hydrochloride mono...	180803101	2
Euro OTC	Lidocaine hydrochloride mono...	12020351612015-01	1
Euro OTC	Lidocaine hydrochloride mono...	1066024-01	1
Euro OTC	Lidocaine hydrochloride mono...	1606024-02	48
Euro/ Anzag	Lidocaine hydrochloride mono...	1606024-03	1
Euro/Alliance Healthcare	Lidocaine hydrochloride mono...	150523-01	1
Euro OTC	Lidocaine hydrochloride mono...	1606024_02	2
Euro/Phönix	Lidocaine hydrochloride mono...	141101010-01	1
Euro/Phönix	Lidocaine hydrochloride mono...	1612015-01	1
Euro/Phönix	Lidocaine hydrochloride mono...	1808031-03	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Lidocaine hydrochloride mono...	1505023-01	64
Euro OTC	Lidocaine hydrochloride mono...	1010024-01	2
Euro OTC	Lidocaine hydrochloride mono...	2805016-01	1
Euro OTC	Lidocaine hydrochloride mono...	141101001	4
Euro OTC	Lidocaine hydrochloride mono...	1202035	1
Euro OTC	Lidocaine hydrochloride mono...	1202035-02	35
Euro OTC	Lidocaine hydrochloride mono...	1612015-02	45
Euro OTC	Lidocaine hydrochloride mono...	1505023-02	19
Euro OTC	Lidocaine hydrochloride mono...	1612015-01	33
Euro OTC	Lidocaine hydrochloride mono...	190701201	1
Euro OTC	Lidocaine hydrochloride mono...	LDH/116023	1
Europ Ots Pharma	Lidocaine hydrochloride mono...	1403025-01	1
Fagon	Lidocaine hydrochloride mono...	15/17-B01-316805	1
Fagron	Lidocaine hydrochloride mono...	1505023-01	2
Fagron	Lidocaine hydrochloride mono...	11L09-N09	2
Fagron	Lidocaine hydrochloride mono...	8F26-N07	1
Fagron	Lidocaine hydrochloride mono...	12c05-N02	1
Fagron	Lidocaine hydrochloride mono...	12E14-N04	2
Fagron	Lidocaine hydrochloride mono...	13F07-N06	7
Fagron	Lidocaine hydrochloride mono...	9B3M1L2Fo118	1
Fagron	Lidocaine hydrochloride mono...	13F07N06	1
Fagron	Lidocaine hydrochloride mono...	14B12-B03-292214	9
Fagron	Lidocaine hydrochloride mono...	1202035-02	1
Fagron	Lidocaine hydrochloride mono...	14e13-b06-294975	1
Fagron	Lidocaine hydrochloride mono...	14J07-B04-299433	4
Fagron	Lidocaine hydrochloride mono...	14e13-b06-294973	1
Fagron	Lidocaine hydrochloride mono...	14J07-B04-299434	2
Fagron	Lidocaine hydrochloride mono...	14J20-B05-303133	2
Fagron	Lidocaine hydrochloride mono...	14j20-b05-303133	1
Fagron	Lidocaine hydrochloride mono...	16C09-B03-322144	4
Fagron	Lidocaine hydrochloride mono...	161201501	1
Fagron	Lidocaine hydrochloride mono...	218I-01775	1
Fagron	Lidocaine hydrochloride mono...	1612015-01	1
Fagron	Lidocaine hydrochloride mono...	17G10-B08-346659	2
Fagron	Lidocaine hydrochloride mono...	168020-0001	1
Fagron	Lidocaine hydrochloride mono...	18B23-B03-352117	3
Fagron	Lidocaine hydrochloride mono...	18B23-B03	2
Fagron	Lidocaine hydrochloride mono...	1808031-01	1
Fagron	Lidocaine hydrochloride mono...	17A16-B07-331959	3
Fagron	Lidocaine hydrochloride mono...	17G10-B08-342287	1
Fagron	Lidocaine hydrochloride mono...	18B23-B03-348590	3
Fagron	Lidocaine hydrochloride mono...	9E08-N03	1
Fagron	Lidocaine hydrochloride mono...	15/17-B01-316805	5
Fagron	Lidocaine hydrochloride mono...	LDH/116037	2
Fagron	Lidocaine hydrochloride mono...	14J20-B05-303131	2
Fagron	Lidocaine hydrochloride mono...	14J20-b05	1
Fagron	Lidocaine hydrochloride mono...	14E13-B06-294975	5
Fagron	Lidocaine hydrochloride mono...	13L18-B11-286901	1
Fagron	Lidocaine hydrochloride mono...	15I17-b01-316805	1
Fagron	Lidocaine hydrochloride mono...	1420-b05-303	1
Fagron	Lidocaine hydrochloride mono...	16C09-B03-319230	1
Fagron	Lidocaine hydrochloride mono...	17A16-B07-333010	4
Fagron	Lidocaine hydrochloride mono...	1612015-02	3
Fagron	Lidocaine hydrochloride mono...	16C09-B03	1
Fagron	Lidocaine hydrochloride mono...	15/17-B01316805	1
Fagron	Lidocaine hydrochloride mono...	15I17-B01-315828	2
Fagron	Lidocaine hydrochloride mono...	15215311	2
Fagron	Lidocaine hydrochloride mono...	12C05-N02	1
Fagron	Lidocaine hydrochloride mono...	4612Q-01775	1
Fagron	Lidocaine hydrochloride mono...	15I17-B01-316805	2

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Supplier	Substance	Batch	Spectra
Fagron	Lidocaine hydrochloride mono...	1517-801	1
Fagron	Lidocaine hydrochloride mono...	15/17-b01-315828	1
Fagron	Lidocaine hydrochloride mono...	15299513	1
Fagron	Lidocaine hydrochloride mono...	1517-B01	1
Fagron	Lidocaine hydrochloride mono...	17A16-B07	1
Fagron	Lidocaine hydrochloride mono...	LDH/116023	1
Fagron	Lidocaine hydrochloride mono...	17G10-B08-346659	1
Fagron	Lidocaine hydrochloride mono...	14/20-B05	1
Fagron	Lidocaine hydrochloride mono...	16J24-B15-329421	1
Fargon GmbH & Co.KG	Lidocaine hydrochloride mono...	15/17-B01-316805	1
Fargon GmbH & Co.KG	Lidocaine hydrochloride mono...	16C09-B03-322144	2
Fiebig	Lidocaine hydrochloride mono...	1808031-01	1
Fiebig 04.7.13 EK 4,54	Lidocaine hydrochloride mono...	12135511	1
Finze	Lidocaine hydrochloride mono...	1202035-01	1
Frago/Noweda	Lidocaine hydrochloride mono...	6108-05-0	1
Gatt-Koller	Lidocaine hydrochloride mono...	1801084	1
Gehe	Lidocaine hydrochloride mono...	12C05-N02	2
Gehe	Lidocaine hydrochloride mono...	1190313	1
Gehe	Lidocaine hydrochloride mono...	1202035-02	1
Gehe	Lidocaine hydrochloride mono...	1411010-01	1
Gehe	Lidocaine hydrochloride mono...	15215304	1
Gehe	Lidocaine hydrochloride mono...	15299516	1
Gehe	Lidocaine hydrochloride mono...	1606024-02	1
Gehe	Lidocaine hydrochloride mono...	1612015-02	1
Gehe	Lidocaine hydrochloride mono...	LDH/116023	1
Gehe	Lidocaine hydrochloride mono...	1808031-01	1
Gehe	Lidocaine hydrochloride mono...	1808031-02	1
GEHE	Lidocaine hydrochloride mono...	1612015-01	1
GEHE	Lidocaine hydrochloride mono...	1606024-02	1
GEHE	Lidocaine hydrochloride mono...	16222214	1
GEHE	Lidocaine hydrochloride mono...	1612015-02	1
GEHE	Lidocaine hydrochloride mono...	17292312	1
Caelo	Lidocaine hydrochloride mono...	1517-B01-315828	1
Caelo	Lidocaine hydrochloride mono...	168020-0003	1
Bombastus	Lidocaine hydrochloride mono...	1606024-01	6
Caelo	Lidocaine hydrochloride mono...	14J20-B05-303133	1
Gehe/Euro	Lidocaine hydrochloride mono...	1612015-02	1
Hedinger/Ebert	Lidocaine hydrochloride mono...	13118807	1
Euro OTC	Lidocaine hydrochloride mono...	LDH/719007	1
Kehr	Lidocaine hydrochloride mono...	1606024-02	1
Kehr	Lidocaine hydrochloride mono...	1612015-01	1
Kehr	Lidocaine hydrochloride mono...	1612015-02	1
Kehr	Lidocaine hydrochloride mono...	1612015-03	1
Klenk	Lidocaine hydrochloride mono...	1612015-01	2
kögl	Lidocaine hydrochloride mono...	1803832	1
Konduskar/Phönix	Lidocaine hydrochloride mono...	1202035-03	1
L10	Lidocaine hydrochloride mono...	1612015-01	1
L10	Lidocaine hydrochloride mono...	1612015-03	1
L12	Lidocaine hydrochloride mono...	1606024-01	2
L12	Lidocaine hydrochloride mono...	1505023-02	1
Mahendra Chem.	Lidocaine hydrochloride mono...	1411010-01	1
Mahendra Chem./ Phönix ...	Lidocaine hydrochloride mono...	1411010-01	1
Mahendra Chem./Noweda	Lidocaine hydrochloride mono...	1505023	1
Noweda	Lidocaine hydrochloride mono...	1108017-02	1
Noweda	Lidocaine hydrochloride mono...	1202035-03	1
Noweda	Lidocaine hydrochloride mono...	141101002	1
Noweda	Lidocaine hydrochloride mono...	16222207	2
Noweda	Lidocaine hydrochloride mono...	1606024-02	1
Noweda	Lidocaine hydrochloride mono...	16222214	1
Noweda	Lidocaine hydrochloride mono...	1812015-04	1

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Supplier	Substance	Batch	Spectra
Noweda	Lidocaine hydrochloride mono...	1612015-05	1
Noweda 04.12.2019	Lidocaine hydrochloride mono...	907012-01	1
Noweda 23.10.2019	Lidocaine hydrochloride mono...	1808031-03	1
Noweda/EuRo	Lidocaine hydrochloride mono...	1612015-03	1
Euro OTC	Lidocaine hydrochloride mono...	1600024-02	1
Noweda 31.07.2019	Lidocaine hydrochloride mono...	1808031-02	1
Euro OTC	Lidocaine hydrochloride mono...	1808031-01	51
Fagron	Lidocaine hydrochloride mono...	15299516	1
Phoenix	Lidocaine hydrochloride mono...	16C09-B03-322144	1
Phoenix	Lidocaine hydrochloride mono...	3238	1
Phoenix	Lidocaine hydrochloride mono...	1808031-01	1
Phoenix	Lidocaine hydrochloride mono...	1612015-02	1
Phoenix	Lidocaine hydrochloride mono...	1808031-02	3
Phoenix	Lidocaine hydrochloride mono...	1808031-03	1
Phoenix 03.12.2018	Lidocaine hydrochloride mono...	1808031-01	1
PHOENIX 17.06.2014	Lidocaine hydrochloride mono...	1403025-01	1
Phoenix 26.02.2014	Lidocaine hydrochloride mono...	13118814	1
PHOENIX am 12.02.2014	Lidocaine hydrochloride mono...	1202035-02	1
phönix	Lidocaine hydrochloride mono...	1505023-03	1
phönix	Lidocaine hydrochloride mono...	16222207	2
Phönix	Lidocaine hydrochloride mono...	12176103	1
Phönix	Lidocaine hydrochloride mono...	1202035-03	1
Phönix	Lidocaine hydrochloride mono...	1606024-01	1
Phönix	Lidocaine hydrochloride mono...	1612015-03	1
Phönix Gotha	Lidocaine hydrochloride mono...	1411010-02	1
Phönix/apo ident	Lidocaine hydrochloride mono...	1808031-01	1
Caelo	Lidocaine hydrochloride mono...	13118807	6
Rondell Apotheke	Lidocaine hydrochloride mono...	15215308	1
sana	Lidocaine hydrochloride mono...	1403025-02	1
Sanacorp	Lidocaine hydrochloride mono...	1202035-01	3
Sanacorp	Lidocaine hydrochloride mono...	13118807	1
Sanacorp	Lidocaine hydrochloride mono...	14J07-B04-299434	2
Sanacorp	Lidocaine hydrochloride mono...	15215309	1
Sanacorp	Lidocaine hydrochloride mono...	150502302	1
Sanacorp	Lidocaine hydrochloride mono...	15215312	1
Sanacorp	Lidocaine hydrochloride mono...	17204804	1
Caelo	Lidocaine hydrochloride mono...	13343007	12
Fagron	Lidocaine hydrochloride mono...	11H18-N01	1
Caelo	Lidocaine hydrochloride mono...	11302906	3
Caelo	Lidocaine hydrochloride mono...	AKD14	1
siehe Protokoll	Lidocaine hydrochloride mono...	1606024-01	1
Swati	Lidocaine hydrochloride mono...	1606024-01	1
Swati / Noweda	Lidocaine hydrochloride mono...	1606024-01	1
Swati/Noweda	Lidocaine hydrochloride mono...	LDH/116007	1
Symbiotica	Lidocaine hydrochloride mono...	1606024-02	1
Caelo	Lidocaine hydrochloride mono...	12135511	2
Caelo	Lidocaine hydrochloride mono...		1
Euro OTC	Lidocaine hydrochloride mono...	1403025-02	14
Euro OTC	Lidocaine hydrochloride mono...		3
Moehs Catalana, S.L./Ph...	Lidocaine hydrochloride mono...		1

- 109 793 spectra from 742 *Apo-Ident* customers from a total of 31 607 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lidocaine hydrochloride monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lidocaine hydrochloride monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	240	0	118 902
Type C	0	1451	3	109 793

The substance/substance group *Lidocaine hydrochloride monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	99.7937 % (> 99.5873 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lidocaine hydrochloride monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fluocinoloneacetonid, micronized	42.94	—
Methylprednisolone	43.74	—
Prednisolone acetate	59.27	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lidocaine hydrochloride monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20882	20882	0.00	46.62
21613	23807	4.74	43.74
21770	21770	0.00	47.09
23807	23807	0.00	43.92
24776	24776	0.00	48.02

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Lithium orotate monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21055-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lithium orotate monohydrate; Lithii orotas monohydricim

Special notes

When selecting the *Lithium orotate monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lithium orotate monohydrate	4	2	1

Second-stage model

For differentiation of the substance/substance group *Lithium orotate monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lithium orotate monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Lithium orotate ...	13J04-N01	21055	40	1405616
Fagron	Lithium orotate ...	13I09-B04-290311	21688	60	20130927
Fagron	Lithium orotate ...	15F25-B01-315219	22502	40	20150716
Fagron	Lithium orotate ...	18K21-B01-363417	25063	40	20181231

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Lithium orotate monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Lithium orotate monohydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Lithium orotate monohydrate	16D15-B08-321402	23269	40
Fagron	Lithium orotate monohydrate	18A19-B12-347442	24111	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 1 *Apo-Ident* customers from 2 batches from the substance/substance group *Lithium orotate monohydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Pfannenschmidt	Lithium orotate monohydrate	ORL00212	1
Fagron	Lithium orotate monohydrate	13J04-N01	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lithium orotate monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lithium orotate monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	80	0	119 062
Type C	0	2	0	111 245

The substance/substance group *Lithium orotate monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lithium orotate monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium orotate dihydrate	66.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lithium orotate monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21055	21055	0.00	82.01
21688	21055	1.72	81.77
22502	21055	5.12	82.30
25063	21055	8.78	83.11

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-leucine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20970-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-leucine; Leucinum

Special notes

When selecting the *L-leucine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-leucine	4	2	4

Second-stage model

For differentiation of the substance/substance group *L-leucine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-leucine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	L-leucine	1302013-01	21612	60	20130320
Euro OTC	L-leucine	1601032	22380	40	20160308*
Fagron	L-leucine	13J09-N03	20970	40	1402431
Fagron	L-leucine	15D09-B06-322249	23199	40	20151030

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *L-leucine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *L-leucine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-leucine	1708010	23607	40
Euro OTC	L-leucine	1901008	24473	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *L-leucine*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	L-leucine	1708010-01	2
Euro OTC	L-leucine	700113	1
Euro OTC	L-leucine	1312032-01	1
Fargon	L-leucine	8160410903	1

- 111 242 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-leucine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-leucine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	80	0	119 062
Type C	0	5	0	111 242

The substance/substance group *L-leucine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group L-leucine in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Isoleucine	38.02	—
Methionine	45.42	—
Levocarnitine	58.44	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-leucine is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20970	20970	0.00	58.50
21612	20970	3.61	60.17
22380	22380	0.00	58.87
23199	22380	8.57	61.35

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-malic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22357-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-malic acid; Acidum-(L)-malicum

Special notes

When selecting the *L-malic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-malic acid	2	1	0

Second-stage model

For differentiation of the substance/substance group *L-malic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-malic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	L-malic acid	15J09-B03-313987	22357	60	9346
Fagron	L-malic acid	15J09-B03-313987	22612	40	20151106
Fagron	L-malic acid	15J09-B03-313987	22730	40	20151106
Fagron	L-malic acid	16J06-B98-327269	23107	40	20161117
Fagron	L-malic acid	16J06-B98-327269	23222	40	20161117

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *L-malic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 469 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *L-malic acid*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	L-malic acid	17E23-B03-335458	23762	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *L-malic acid*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-malic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-malic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *L-malic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *L-malic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Folic acid hydrate	49.89	—
Acetylcysteine	68.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-malic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22357	22357	0.00	73.92
22612	22357	3.51	72.12
22730	22357	2.70	70.90
23107	22357	1.93	71.58
23222	22357	2.34	72.70

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-phenylalanine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21661-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-phenylalanine; Phenylalaninum

Special notes

When selecting the *L-phenylalanine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-phenylalanine	6	3	2

Second-stage model

For differentiation of the substance/substance group *L-phenylalanine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-phenylalanine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	L-phenylalanine	14088304	21661	60	1501656
Euro OTC	L-phenylalanine	1212014-03	21681	60	20130111
Euro OTC	L-phenylalanine	1704003	23173	40	20170425*
Euro OTC	L-phenylalanine	1909032	24985	40	20191017*
Fagron	L-phenylalanine	17B13-B03-343288	23936	40	20170309
Fagron	L-phenylalanine	19J23-F10-366142	24951	40	20191127

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *L-phenylalanine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *L-phenylalanine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-phenylalanine	1409013-02	23024	40
Euro OTC	L-phenylalanine	1808022	24198	40
Euro OTC	L-phenylalanine	1907032	24846	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 5 *Apo-Ident* customers from 2 batches from the substance/substance group *L-phenylalanine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	L-phenylalanine	1704003-02	1
Euro OTC	L-phenylalanine	1409013-02	12

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-phenylalanine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-phenylalanine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	116	4	119 022
Type C	0	10	3	111 234

The substance/substance group *L-phenylalanine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	96.6667 % (> 94.1667 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *L-phenylalanine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Doxylamine hydrogen succinate	26.67	—
Ethyl hydrogen fumarate calcium	35.47	—
Midazolam hydrochloride	37.86	—
Naphazoline hydrochloride	40.83	—
L-tryptophan	43.01	—
Griseofulvin	49.48	—
Indometacin	58.99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-phenylalanine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21661	21661	0.00	61.16
21681	23173	14.48	72.23
23936	21661	3.62	63.41
24951	21661	6.80	61.63
24985	24985	0.00	50.93
23173	23173	0.00	78.79

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-proline**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21034-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-proline; Prolinum

Special notes

When selecting the *L-proline* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-proline	4	6	1

Second-stage model

For differentiation of the substance/substance group *L-proline* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-proline*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	L-proline	1606010	22677	40	20160714*
Euro OTC	L-proline	1705021	23546	40	20170720*
Fagron	L-proline	15D13-B02-308152	22270	60	1704059
Fagron	L-proline	16J14-B01-327195	23109	40	20161116

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *L-proline*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 340 spectra of 8 reference samples from the substance/substance group *L-proline*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-proline	L1210046-02	21034	40
Euro OTC	L-proline	L1210046-01	21103	40
Euro OTC	L-proline	1606010-01	23013	40
Euro OTC	L-proline	1801047	23961	40
Euro OTC	L-proline	1812009	24419	40
Euro OTC	L-proline	1909002	24844	40
Euro OTC	L-proline	L1210046-02	21075	60
Euro OTC	L-proline	1606010-01	23100	40

- 118 802 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *L-proline*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	L-proline	L1210046-03	1

- 111 246 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-proline* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-proline* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	259	81	118 802
Type C	0	1	0	111 246

The substance/substance group *L-proline* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	76.1765 % (> 75.2941 %)
Type C	100.0000 % (> 99.8911 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group L-proline in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	24.06	—
Omeprazole	26.30	—
Glycine	30.21	—
Diltiazem hydrochloride	41.58	—
Mometasone furoate, micronized	50.81	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group L-proline is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23546	23546	0.00	28.06
22677	22677	0.00	41.65
22270	22270	0.00	26.30
23109	22270	3.30	27.40

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-threonine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20734-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-threonine; Threoninum

Special notes

When selecting the *L-threonine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-threonine	4	5	2

Second-stage model

For differentiation of the substance/substance group *L-threonine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-threonine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	L-threonine	1210027-01	21033	40	1403152
Euro OTC	L-threonine	1210027-01	22319	60	20121108
Euro OTC	L-threonine	1601031	22378	40	20160225*
Euro OTC	L-threonine	1909003	24850	40	20190913*
Fagron	L-threonine	12H02-N03	20734	40	1402580

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *L-threonine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *L-threonine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-threonine	1606019	22679	40
Euro OTC	L-threonine	1609014	22792	40
Euro OTC	L-threonine	1703035	23158	40
Euro OTC	L-threonine	1711010	23738	40
Euro OTC	L-threonine	1811030	24417	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *L-threonine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	L-threonine	1606019-02	1
Fargon	L-threonine	2114720407	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-threonine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-threonine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	200	0	118 942
Type C	0	2	0	111 245

The substance/substance group *L-threonine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *L-threonine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	47.69	—
Histamine dihydrochloride	48.02	—
5-aminolevulinic acid hydrochloride	52.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-threonine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20734	20734	0.00	54.28
21033	21033	0.00	52.08
22319	22378	7.71	54.16
22378	22378	0.00	54.90
24850	24850	0.00	53.37

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **L-tryptophan**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20336-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

L-tryptophan; Tryptophanum

Special notes

When selecting the *L-tryptophan* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
L-tryptophan	5	4	7

Second-stage model

For differentiation of the substance/substance group *L-tryptophan* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *L-tryptophan*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	L-tryptophan	1506003	21866	60	20150630*
Euro OTC	L-tryptophan	1506003	21871	60	20150630*
Euro OTC	L-tryptophan	1712006	23876	40	20180105*
Euro OTC	L-tryptophan	1910016	24972	40	20191106*
Fagron	L-tryptophan	14B05-B32-293485	21784	60	AR-15-FG-009473-01
Fagron	L-tryptophan	17G19-B01-343931	23998	40	20170919

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *L-tryptophan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 389 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *L-tryptophan*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	L-tryotophan	1806006	24144	40
Euro OTC	L-tryotophan	1812002	24426	40
Euro OTC	L-tryotophan	1906018	24795	40
Fagron	L-tryotophan	16E11-B03-322919	23195	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 4 *Apo-Ident* customers from 7 batches from the substance/substance group *L-tryotophan*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	L-tryotophan	131046	1
Euro OTC	L-tryotophan	150600302	1
Euro OTC	L-tryotophan	180600601	1
Euro OTC	L-tryotophan	1506003-03	2
Euro OTC	L-tryotophan	1712006-01	1
euroct/gehe	L-tryotophan	1212010-01	5
Euro OTC	L-tryotophan	1307004-01	2

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *L-tryotophan* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *L-tryotophan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	160	0	118 982
Type C	0	13	0	111 234

The substance/substance group *L-tryotophan* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *L-tryptophan* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dithranol	26.76	—
Midazolam hydrochloride	37.47	—
Doxylamine hydrogen succinate	58.67	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *L-tryptophan* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21784	21784	0.00	26.85
21866	21866	0.00	29.82
21871	21871	0.00	29.11
23876	23876	0.00	30.23
23998	24972	2.35	29.78
24972	24972	0.00	29.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Lysine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20385-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Lysine hydrochloride; Lysine HCl; Lysini hydrochloridum

Special notes

When selecting the *Lysine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Lysine hydrochloride	6	4	2

Second-stage model

For differentiation of the substance/substance group *Lysine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Lysine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Lysine hydrochlo...	1611021	22865	40	20161202*
Euro OTC	Lysine hydrochlo...	1708009	23698	40	20170922*
Euro OTC	Lysine hydrochlo...	1805030	24123	40	20180611*
Euro OTC	Lysine hydrochlo...	2003009	25128	40	20200403*
Fagron	Lysine hydrochlo...	15B09-B06-304170	21963	60	20150220
Fagron	Lysine hydrochlo...	14H20-B03-301894	21983	60	AR-16-FG-005856-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Lysine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Lysine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Lysine hydrochloride	1603011	22527	40
Euro OTC	Lysine hydrochloride	1902008	24622	40
Euro OTC	Lysine hydrochloride	1907038	24809	40
Fagron	Lysine hydrochloride	12B14-N08	20735	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Lysine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Lysine hydrochloride	1708009-01	2
Euro OTC	Lysine hydrochloride	1805030-01	1
Fagron	Lysine hydrochloride	14H20-B03-301894	1

- 111 243 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Lysine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lysine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	120	40	118 982
Type C	0	4	0	111 243

The substance/substance group *Lysine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	75.0000 % (> 73.1250 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lysine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cystine	49.39	—
Glycine	69.84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lysine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21963	23698	3.18	55.62
21983	21983	0.00	57.10
22865	22865	0.00	57.80
23698	23698	0.00	55.39
24123	24123	0.00	52.21
25128	25128	0.00	56.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Macrogols 1500**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20112-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Macrogols 1500; Macrogolum 1500

Special notes

When selecting the *Macrogols 1500* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Macrogols 1500	5	6	29

Second-stage model

For differentiation of the substance/substance group *Macrogols 1500* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Macrogols 1500*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Macrogols 1500	12324607	20977	40	1403323
Caelo	Macrogols 1500	17120001	23241	40	20170519
Caelo	Macrogols 1500	171200	23291	40	20170519*
Euro OTC	Macrogols 1500	1508002	21948	60	20150810*
Euro OTC	Macrogols 1500	1604005	22544	40	20160512*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Macrogols 1500*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Macrogols 1500*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Macrogols 1500	172221	23625	40
Caelo	Macrogols 1500	182290	24350	40
Euro OTC	Macrogols 1500	1705004	23423	40
Euro OTC	Macrogols 1500	1705036	23440	40
Euro OTC	Macrogols 1500	1711032	23898	40
Euro OTC	Macrogols 1500	1806015	24147	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 55 spectra from 22 *Apo-Ident* customers from 30 batches from the substance/substance group *Macrogols 1500*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM / Herba	Macrogols 1500	KN-0826/10	1
Caelo	Macrogols 1500	14072409	1
Caelo	Macrogols 1500	10105901	1
Caelo	Macrogols 1500	11071309	1
Caelo	Macrogols 1500	13140902	2
Caelo	Macrogols 1500	14072412	1
Caelo	Macrogols 1500	15120007	1
Caelo	Macrogols 1500	15413101	1
Caelo	Macrogols 1500	15413105	5
Caelo	Macrogols 1500	16138407	1
Caelo	Macrogols 1500	17120002	2
Caelo	Macrogols 1500	18129503	1
Caelo	Macrogols 1500	1812905	1
Caelo	Macrogols 1500	18129506	1
Caelo	Macrogols 1500	17120011	1
Caelo	Macrogols 1500	13140906	1
Caelo	Macrogols 1500	18129505	1
Caelo	Macrogols 1500	15413111	1
Caelo	Macrogols 1500	12109409	1
Caelo	Macrogols 1500	13140901	1
Caelo	Macrogols 1500	18045703	1
Euro OTC	Macrogols 1500	1503026-01	4
Euro OTC	Macrogols 1500	1103017-02	4
Euro OTC	Macrogols 1500	1206005-01	5
Euro OTC	Macrogols 1500	1304023-01	7
Euro OTC	Macrogols 1500	1406004-01	2
Gehe	Macrogols 1500	14072409	1
Caelo	Macrogols 1500	18229004	1
Krieger	Macrogols 1500	1712002	1
phoenix	Macrogols 1500	18229004	1
Phönix	Macrogols 1500	14072402	1
Caelo	Macrogols 1500	17120001	1

- 111 192 spectra from 742 *Apo-Ident* customers from a total of 31 862 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Macrogols 1500* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Macrogols 1500* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	214	26	118 902
Type C	0	52	3	111 192

The substance/substance group *Macrogols 1500* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	89.1667 % (> 87.9167 %)
Type C	100.0000 % (> 99.8899 %)	94.5455 % (> 89.0909 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Macrogols 1500* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Macrogols 4000	27.94	—
Emulsifying cetostearyl alcohol (type A)	55.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Macrogols 1500* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21948	21948	0.00	41.21
22544	22544	0.00	48.60
20977	20977	0.00	33.47
23241	23291	6.30	33.13
23291	23291	0.00	32.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Macrogols 4000**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20690-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Macrogols 4000; Macrogolum 4000

Special notes

When selecting the *Macrogols 4000* substance/substance group, the following information is displayed to the user:

- Advice for the distinction from Macrogol 6000: Macrogol 4000 cannot be certainly distinct from Macrogol 6000, which is however currently not deliverable in Germany. Please decide, if an additional analysis seems reasonable.

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Macrogols 4000	12	21	312

Second-stage model

For differentiation of the substance/substance group *Macrogols 4000* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Macrogols 4000*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Macrogols 4000	12074116	20690	40	1401164
Caelo	Macrogols 4000	12318019	20975	40	1403322
Caelo	Macrogols 4000	12361502	21065	40	20130107
Caelo	Macrogols 4000	13356616	21357	40	20131107
Euro OTC	Macrogols 4000	1507004	21841	60	0000010550
Euro OTC	Macrogols 4000	1508031	21903	60	20150914*
Euro OTC	Macrogols 4000	1605012	22567	40	20160606*
Euro OTC	Macrogols 4000	1605025	22570	40	20160603*
Euro OTC	Macrogols 4000	1702003	23174	40	20170301*
Euro OTC	Macrogols 4000	1711016	23902	40	20171214*
Fagron	Macrogols 4000	15B13-B04-305461	21886	60	AR-16-FG-004020-01
Fagron	Macrogols 4000	16F10-B04-325645	23021	40	20160822

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 540 spectra of 12 reference samples from the substance/substance group *Macrogols 4000*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 110 149 spectra from a total of 1954 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 840 spectra of 21 reference samples from the substance/substance group *Macrogols 4000*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Macrogols 4000	11172433	20692	40
Caelo	Macrogols 4000	170686	23280	40
Caelo	Macrogols 4000	171190	23282	40
Caelo	Macrogols 4000	172081	23657	40
Caelo	Macrogols 4000	173039	23825	40
Caelo	Macrogols 4000	181974	24227	40
Caelo	Macrogols 4000	182154	24229	40
Caelo	Macrogols 4000	182448	24352	40
Caelo	Macrogols 4000	183153	24360	40
Caelo	Macrogols 4000	190093	24564	40
Caelo	Macrogols 4000	191756	24743	40
Euro OTC	Macrogols 4000	1609018	22791	40
Euro OTC	Macrogols 4000	1701007	22983	40
Euro OTC	Macrogols 4000	1705019	23433	40
Euro OTC	Macrogols 4000	1707026	23537	40
Euro OTC	Macrogols 4000	1804001	24089	40
Euro OTC	Macrogols 4000	1803029	24094	40
Euro OTC	Macrogols 4000	1810003	24339	40
Euro OTC	Macrogols 4000	1902009	24463	40
Euro OTC	Macrogols 4000	1907002	24798	40
Euro OTC	Macrogols 4000	1911027	25073	40

- 118302 spectra from a total of 2399 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 774 spectra from 236 *Apo-Ident* customers from 319 batches from the substance/substance group *Macrogols 4000*.
- Among them are spectra of independent samples from 312 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Macrogols 4000	KNC0366J15	2
AHD	Macrogols 4000	14L12-B06-301991	2
AHD	Macrogols 4000	15G15B07-313592	1
AHD	Macrogols 4000	17E02-B03	1
AHD	Macrogols 4000	17E02-B03-335507	3
AHD	Macrogols 4000	17208106	1
AHD	Macrogols 4000	16K25-B02-330527	3
AHD	Macrogols 4000	11H11-B05340782	1

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Supplier	Substance	Batch	Spectra
AHD	Macrogols 4000	17K06-B05-345076	1
AHD	Macrogols 4000	17K06-B05	2
AHD	Macrogols 4000	18G30-B01	2
AHD	Macrogols 4000	18G30-B01-352394	2
Fagron	Macrogols 4000	16A20-B15-320060	1
Alliance	Macrogols 4000	18215403	1
Alliance Healthcare	Macrogols 4000	12361512	2
Fagron	Macrogols 4000	12F29-N01	2
Fagron	Macrogols 4000	13F12-N09	1
Fagron	Macrogols 4000	14A03-B01-289602	3
Fagron	Macrogols 4000	14D14-B06-293453	2
Fagron	Macrogols 4000	14K03-B07-300522	2
Anzag	Macrogols 4000	17068603	1
ANZAG 15.05.2014	Macrogols 4000	13356616	1
Bombastus	Macrogols 4000	13136016	1
caedo	Macrogols 4000	17303902	2
Caelo	Macrogols 4000	16308908	3
Caelo	Macrogols 4000	12074109	3
Caelo	Macrogols 4000	1172404	1
Caelo	Macrogols 4000	12149108	1
Caelo	Macrogols 4000	12074102	1
Caelo	Macrogols 4000	12149113	2
Caelo	Macrogols 4000	12361513	3
Caelo	Macrogols 4000	12361512	2
Caelo	Macrogols 4000	3940608	1
Caelo	Macrogols 4000	IntCh217002	1
Caelo	Macrogols 4000	13136003	3
Caelo	Macrogols 4000	13136009	3
Caelo	Macrogols 4000	13136011	4
Caelo	Macrogols 4000	13356601	4
Caelo	Macrogols 4000	13356602	3
Caelo	Macrogols 4000	12074114	1
Caelo	Macrogols 4000	123Test	1
Caelo	Macrogols 4000	14180520	4
Caelo	Macrogols 4000	14180508	2
Caelo	Macrogols 4000	14180522	1
Caelo	Macrogols 4000	14352607	2
Caelo	Macrogols 4000	14352613	5
Caelo	Macrogols 4000	23061505	1
Caelo	Macrogols 4000	13081501	1
Caelo	Macrogols 4000	14196017	1
Caelo	Macrogols 4000	15159502	3
Caelo	Macrogols 4000	15159515	4
Caelo	Macrogols 4000	15159514	4
Caelo	Macrogols 4000	15335001	9
Caelo	Macrogols 4000	15225003	4
Caelo	Macrogols 4000	15335002	3
Caelo	Macrogols 4000	4123585	1
Caelo	Macrogols 4000	16023904	4
Caelo	Macrogols 4000	16023903	5
Caelo	Macrogols 4000	15376515	1
Caelo	Macrogols 4000	160912M	1
Caelo	Macrogols 4000	161017M/15406304	1
Caelo	Macrogols 4000	161202M/16152004	1
Caelo	Macrogols 4000	15376518	1
Caelo	Macrogols 4000	170105M16152004	1
Caelo	Macrogols 4000	16267307	12
Caelo	Macrogols 4000	16308904	7
Caelo	Macrogols 4000	16267308	3
Caelo	Macrogols 4000	16308905	3

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Macrogols 4000	5041701	1
Caelo	Macrogols 4000	1508031-02	1
Caelo	Macrogols 4000	17035603	1
Caelo	Macrogols 4000	17035604	3
Caelo	Macrogols 4000	17035607	3
Caelo	Macrogols 4000	17119005	2
Caelo	Macrogols 4000	17068603	3
Caelo	Macrogols 4000	1720813	1
Caelo	Macrogols 4000	28111706	1
Caelo	Macrogols 4000	17208104	11
Caelo	Macrogols 4000	17208105	1
Caelo	Macrogols 4000	30041803	1
Caelo	Macrogols 4000	18106101	2
Caelo	Macrogols 4000	9061805	1
Caelo	Macrogols 4000	18106104	5
Caelo	Macrogols 4000	18106106	1
Caelo	Macrogols 4000	190920	1
Caelo	Macrogols 4000	17337901	5
Caelo	Macrogols 4000	18244803	3
Caelo	Macrogols 4000	18215403	2
Caelo	Macrogols 4000	19009302	2
Caelo	Macrogols 4000	18315307	8
Caelo	Macrogols 4000	19009308	1
Caelo	Macrogols 4000	19175606	2
Caelo	Macrogols 4000	19142403	2
Caelo	Macrogols 4000	19175605	3
Caelo	Macrogols 4000	19142402	2
Caelo	Macrogols 4000	19227702	2
Caelo	Macrogols 4000	177337906	1
Caelo	Macrogols 4000	13335102	1
Caelo	Macrogols 4000	17303901	9
Caelo	Macrogols 4000	12318027	1
Caelo	Macrogols 4000	13356609	1
Caelo	Macrogols 4000	13335107	1
Caelo	Macrogols 4000	13335120	1
Caelo	Macrogols 4000	14196013	1
Caelo	Macrogols 4000	17303903	1
Caelo	Macrogols 4000	17337906	1
Caelo	Macrogols 4000	170529M/16267308	1
Caelo	Macrogols 4000	170612M/17035603	1
Caelo	Macrogols 4000	170710M/17035603	1
Caelo	Macrogols 4000	170817M/17035603	1
Caelo	Macrogols 4000	171211M/17119003	1
Caelo	Macrogols 4000	18106105	21
Caelo	Macrogols 4000	16308907	11
Caelo	Macrogols 4000	18244805	8
Caelo	Macrogols 4000	18315303	4
Caelo	Macrogols 4000	18315305	5
Caelo	Macrogols 4000	16358101	2
Caelo	Macrogols 4000	17119001	2
Caelo	Macrogols 4000	1234	1
Caelo	Macrogols 4000	18215404	3
Caelo	Macrogols 4000	14352618	1
Caelo	Macrogols 4000	1180513	1
Caelo	Macrogols 4000	14196007	1
Caelo	Macrogols 4000	13335106	1
Caelo	Macrogols 4000	14180525	3
Caelo	Macrogols 4000	14180511	2
Caelo	Macrogols 4000	16267308/170227M	1
Caelo	Macrogols 4000	170324M/16267308	1

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Supplier	Substance	Batch	Spectra
Caelo	Macrogols 4000	1010023-02	1
Caelo	Macrogols 4000	12361518	3
Caelo	Macrogols 4000	1401708	1
Caelo	Macrogols 4000	143526	1
Caelo	Macrogols 4000	13136001	3
Caelo	Macrogols 4000	18244809	1
Caelo	Macrogols 4000	18244806	2
Caelo	Macrogols 4000	19227703	1
Caelo	Macrogols 4000	14180504	1
Caelo	Macrogols 4000	39393137	1
Caelo	Macrogols 4000	14352608	1
Caelo	Macrogols 4000	14352614	1
Caelo	Macrogols 4000	16308902	9
Caelo	Macrogols 4000	171103M/17119002	1
Caelo	Macrogols 4000	18215405	2
Caelo	Macrogols 4000	18315304	5
Caelo	Macrogols 4000	19142404	1
Caelo	Macrogols 4000	15406303	3
Caelo	Macrogols 4000	19175604	1
Caelo	Macrogols 4000	192227702	1
Caelo	Macrogols 4000	14061713	1
Caelo	Macrogols 4000	15225001	1
Caelo	Macrogols 4000	17208106	1
Caelo	Macrogols 4000	17035608	1
Caelo	Macrogols 4000	12318011	1
Caelo	Macrogols 4000	13356611	2
Caelo	Macrogols 4000	13356617	6
Caelo	Macrogols 4000	14061708	9
Caelo	Macrogols 4000	14180503	1
Caelo	Macrogols 4000	14180524	1
Caelo	Macrogols 4000	14352611	2
Caelo	Macrogols 4000	15159504	3
Caelo	Macrogols 4000	15335007	4
Caelo	Macrogols 4000	15406302	2
Caelo	Macrogols 4000	16152002	1
Caelo	Macrogols 4000	1030517	1
Caelo	Macrogols 4000	1200617/16368105	1
Caelo	Macrogols 4000	18106110	4
Caelo	Macrogols 4000	18244802	8
Caelo	Macrogols 4000	19009305	3
Caelo	Macrogols 4000	19142401	2
Caelo	Macrogols 4000	17035606	9
Caelo	Macrogols 4000	16267305	8
Caelo	Macrogols 4000	170504M/16308906	1
Caelo	Macrogols 4000	170928M/17119002	1
Caelo	Macrogols 4000	17208103	13
Caelo	Macrogols 4000	1720103	1
Caelo	Macrogols 4000	18315301	7
Caelo	Macrogols 4000	16152001	13
Caelo	Macrogols 4000	13136010	1
Caelo	Macrogols 4000	13356621	1
Caelo	Macrogols 4000	19175603	2
Caelo	Macrogols 4000	1316003	1
Caelo	Macrogols 4000	15159516	1
Caelo	Macrogols 4000	16023905	4
Caelo	Macrogols 4000	16152003	4
Caelo	Macrogols 4000	16267311	6
Caelo	Macrogols 4000	16358106	2
Caelo	Macrogols 4000	17303902	7
Caelo	Macrogols 4000	18106103	5

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Supplier	Substance	Batch	Spectra
Caelo	Macrogols 4000	19009313	1
Caelo	Macrogols 4000	11172303	1
Caelo	Macrogols 4000	14061705	5
Caelo	Macrogols 4000	12361506	3
Caelo	Macrogols 4000	14352606	2
Caelo	Macrogols 4000	15335003	6
Caesar & Loretz GmbH	Macrogols 4000	14180520	1
Caesar & Loretz GmbH	Macrogols 4000	18315302	1
Caesar & Loretz GmbH	Macrogols 4000	18244806	1
Caesar & Loretz GmbH	Macrogols 4000	18315303	1
Caesar & Loretz GmbH	Macrogols 4000	18315307	1
Caesar & Loretz GmbH	Macrogols 4000	19009313	1
Caesar & Loretz GmbH	Macrogols 4000	19009308	1
Caesar & Loretz GmbH	Macrogols 4000	19175607	1
Caesar & Loretz GmbH/ AHD	Macrogols 4000	19009302	1
Caesar&Loretz GmbH/ San...	Macrogols 4000	17068603	1
Caesar&Loretz GmbH/Anzag	Macrogols 4000	14196017	1
calo	Macrogols 4000	17303902	1
Cealo/Gehe	Macrogols 4000	16023907	1
DIV GH	Macrogols 4000	13/12	1
EuRho	Macrogols 4000	1206009-01	1
Euro OTC	Macrogols 4000	1810003-01	1
Euro OTC	Macrogols 4000	140701001	1
Euro OTC	Macrogols 4000	1902009-01	2
Euro OTC	Macrogols 4000	17303905	1
Euro OTC	Macrogols 4000	1202040-02	2
Euro OTC	Macrogols 4000	1305020-02	4
Euro OTC	Macrogols 4000	130502002	1
Euro OTC	Macrogols 4000	1005011-01	1
Euro OTC	Macrogols 4000	1808003-01	2
Euro OTC	Macrogols 4000	1508031-01	1
Euro OTC	Macrogols 4000	1507004-01	1
Euro OTC	Macrogols 4000	1508031-02	1
Euro OTC	Macrogols 4000	18315307	1
Euro OTC	Macrogols 4000	15159515	1
Euro OTC	Macrogols 4000	1711016-01	1
Euro OTC	Macrogols 4000	1808003-02	1
Facron	Macrogols 4000	7022014C	1
Fagron	Macrogols 4000	12F29-N01	1
Fagron	Macrogols 4000	12F13-N01	2
Fagron	Macrogols 4000	13B20-N01	2
Fagron	Macrogols 4000	12L10-N06	2
Fagron	Macrogols 4000	13A10-N01	1
Fagron	Macrogols 4000	26082013A	1
Fagron	Macrogols 4000	280913C	2
Fagron	Macrogols 4000	16102013A	1
Fagron	Macrogols 4000	13B20N01	1
Fagron	Macrogols 4000	2122013a	1
Fagron	Macrogols 4000	2122013b	1
Fagron	Macrogols 4000	13G19-N08	2
Fagron	Macrogols 4000	20122013C	1
Fagron	Macrogols 4000	17012014A	1
Fagron	Macrogols 4000	13F12N09	1
Fagron	Macrogols 4000	3032014B	1
Fagron	Macrogols 4000	13130-N03	1
Fagron	Macrogols 4000	160514a	1
Fagron	Macrogols 4000	13I17-N03	1
Fagron	Macrogols 4000	26052014A	1
Fagron	Macrogols 4000	28052014B	1
Fagron	Macrogols 4000	123Test	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Macrogols 4000	14A03B01	1
Fagron	Macrogols 4000	13I30-N03	1
Fagron	Macrogols 4000	18082014C	1
Fagron	Macrogols 4000	25082014A	1
Fagron	Macrogols 4000	15092014A	1
Fagron	Macrogols 4000	20092014A	1
Fagron	Macrogols 4000	13L30-B31	1
Fagron	Macrogols 4000	30092014B	1
Fagron	Macrogols 4000	14K03-_b07-300522	1
Fagron	Macrogols 4000	14D14-B06	1
Fagron	Macrogols 4000	22122014A	1
Fagron	Macrogols 4000	8012015A	1
Fagron	Macrogols 4000	2022015A	1
Fagron	Macrogols 4000	10022015A	1
Fagron	Macrogols 4000	10022015B	1
Fagron	Macrogols 4000	14G15-B07-295632	1
Fagron	Macrogols 4000	505201C	1
Fagron	Macrogols 4000	22062015A	1
Fagron	Macrogols 4000	13G19-N14	1
Fagron	Macrogols 4000	15A08-B03-302762	3
Fagron	Macrogols 4000	15A08B03302762	1
Fagron	Macrogols 4000	14L12-B06	1
Fagron	Macrogols 4000	15G15-B07	1
Fagron	Macrogols 4000	15A08-B03-302761	1
Fagron	Macrogols 4000	15/29-B01-318038	2
Fagron	Macrogols 4000	16A20-B15-320652	6
Fagron	Macrogols 4000	15I29-B01-318038	1
Fagron	Macrogols 4000	16a20-b15-320652	8
Fagron	Macrogols 4000	701014	1
Fagron	Macrogols 4000	19B06-B04-359646	1
Fagron	Macrogols 4000	15G15-B07-313592	2
Fagron	Macrogols 4000	8062015B	1
Fagron	Macrogols 4000	8062015C	1
Fagron	Macrogols 4000	15H10-B04-314037	2
Fagron	Macrogols 4000	21052015A	1
Fagron	Macrogols 4000	12I20-n03	1
Fagron	Macrogols 4000	14A03-B01-289605	1
Fagron	Macrogols 4000	1803029-01	2
Fagron	Macrogols 4000	1112M-02103	1
Fagron	Macrogols 4000	914I-02103	1
Fagron	Macrogols 4000	3114I-02103	1
Fagron	Macrogols 4000	2215I-02103	1
Fagron	Macrogols 4000	16K25-B02-330527	2
Fagron	Macrogols 4000	17K06-B05-345076	2
Fagron	Macrogols 4000	13E22-N03	6
Fagron	Macrogols 4000	14J03-B07300840	1
Fagron	Macrogols 4000	14G21-B04-296899	1
Fagron	Macrogols 4000	14J03-B07-300840	1
Fagron	Macrogols 4000	16152002	1
Fagron	Macrogols 4000	13356608	1
Fagron	Macrogols 4000	290714c	1
Fagron	Macrogols 4000	15H10-B04-31407	1
Fagron	Macrogols 4000	17E02-B03-335507	1
Fagron	Macrogols 4000	18G30-B01	1
Fiebig	Macrogols 4000	14180506	1
Fiebig	Macrogols 4000	13356601	1
Fiebig	Macrogols 4000	15159514	1
Fiebig	Macrogols 4000	16152001	1
Fiebig	Macrogols 4000	16308907	1
Fiebig	Macrogols 4000	17035607	1

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Supplier	Substance	Batch	Spectra
Finteler Apotheke	Macrogols 4000	16308907	2
Finteler Apotheke	Macrogols 4000	17035607	1
Gatt-Koller	Macrogols 4000	1420/04153415	1
Gatt-Koller	Macrogols 4000	1420/04152915	1
Gatt-Koller	Macrogols 4000	2792/07153315	1
Gatt-Koller	Macrogols 4000	4643/01170417	2
Gatt-Koller	Macrogols 4000	1802391	1
Gatt-Koller	Macrogols 4000	1804126	1
Gehe	Macrogols 4000	14K03-B07-300522	1
Gehe	Macrogols 4000	16267307	1
Gehe	Macrogols 4000	17208104	1
Gehe	Macrogols 4000	19175607	1
Gehe	Macrogols 4000	19142401	1
GEHE	Macrogols 4000	18106109	1
Gehe / EuRho	Macrogols 4000	1803029-01	1
GEHE 06.05.2014	Macrogols 4000	13356608	2
Caelo	Macrogols 4000	14J03-B07-304700	3
Caelo	Macrogols 4000	15376519	1
Caelo	Macrogols 4000	1131117/16358107	1
Caelo	Macrogols 4000	1260917/16358105	1
Caelo	Macrogols 4000	16358107/1111217	1
Caelo	Macrogols 4000	16358107	1
Caelo	Macrogols 4000	17337902/1250418	1
Caelo	Macrogols 4000	17337902/1300518	1
Caelo	Macrogols 4000	18106109	3
Fagron	Macrogols 4000	15b03-b08-304701	1
Fagron	Macrogols 4000	15376510	1
Gutenberg-Apotheke	Macrogols 4000	13356609	1
Hedinger	Macrogols 4000	13G19-N08	1
Henry Lamotte	Macrogols 4000	1213test	1
Henry Lamotte Oils GMBH	Macrogols 4000	16267308/170127M	1
Kehr	Macrogols 4000	16308907	1
Kehr	Macrogols 4000	18106105	1
KÖGL	Macrogols 4000	1900232	1
Nachprüfung	Macrogols 4000	14A03-B01-289605	1
Nachtestung-Verlängerung	Macrogols 4000	17/17	1
Noveda	Macrogols 4000	18315307	1
Noweda	Macrogols 4000	12361502	2
Noweda	Macrogols 4000	12361512	1
Noweda	Macrogols 4000	13136003	1
Caelo	Macrogols 4000	14061707	4
Euro OTC	Macrogols 4000	1707026-01	1
Phoenix	Macrogols 4000	12258901	1
Phoenix	Macrogols 4000	16023905	1
Phoenix	Macrogols 4000	18315307	2
Phoenix	Macrogols 4000	19175606	1
Caelo	Macrogols 4000	15406301	7
Caelo	Macrogols 4000	15225013	1
Caelo	Macrogols 4000	17337902/2190218	1
phönix	Macrogols 4000	15406302	1
phönix	Macrogols 4000	1535007	1
phönix	Macrogols 4000	16023904	1
phönix	Macrogols 4000	1502031-02	1
phönix	Macrogols 4000	1605012-01	1
phönix	Macrogols 4000	1701007-01	3
Phönix	Macrogols 4000	1202040-02	1
Phönix	Macrogols 4000	1707026-01	1
Caelo	Macrogols 4000	15376503	3
Rondell Apotheke	Macrogols 4000	16023905	1
Sanacorp	Macrogols 4000	14061707	1

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Supplier	Substance	Batch	Spectra
Sanacorp	Macrogols 4000	15376520	1
Sanacorp	Macrogols 4000	17208104	1
Sanacorp	Macrogols 4000	17303901	1
VDL	Macrogols 4000	16308906	1
WE:Sanacorp 19.10.2016 ...	Macrogols 4000	15406301	2
Fagron	Macrogols 4000	15B13-B04-305461	3
Caelo	Macrogols 4000	12074116	3
Caelo	Macrogols 4000	12361502	3
Caelo	Macrogols 4000	13356616	1
Caelo	Macrogols 4000		1
Caelo	Macrogols 4000	12318019	1

- 110 473 spectra from 742 *Apo-Ident* customers from a total of 31 575 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Macrogols 4000* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Macrogols 4000* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	540	0	110 149
Type B	0	840	0	118 131
Type C	0	768	6	110 470

The substance/substance group *Macrogols 4000* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8889 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.2857 %)
Type C	100.0000 % (> 99.8901 %)	99.2248 % (> 98.8372 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Macrogols 4000* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Macrogols 1500	28.98	–
Emulsifying cetostearyl alcohol (type A)	73.35	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Macrogols 4000* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21903	21903	0.00	40.05
22570	22570	0.00	38.36
23174	23174	0.00	42.35
22567	22567	0.00	41.31
20690	20690	0.00	45.69
21065	21886	7.86	48.13
21357	21886	2.21	43.58
23021	21886	3.82	43.55
20975	20975	0.00	37.40
21841	21841	0.00	30.12
23902	23902	0.00	40.65
21886	21886	0.00	40.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Magnesium citrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20616-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnesium citrate; Magnesii citras

Special notes

When selecting the *Magnesium citrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Magnesium citrate	10	4	5

Second-stage model

For differentiation of the substance/substance group *Magnesium citrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium citrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Magnesium citrate	1501031	21794	60	AR-15-FG-007845-01
Euro OTC	Magnesium citrate	1506020	21829	60	20150623*
Euro OTC	Magnesium citrate	1507019	21860	60	20150722*
Euro OTC	Magnesium citrate	1511018	22225	60	20151130*
Euro OTC	Magnesium citrate	1602028	22505	40	20160314*
Euro OTC	Magnesium citrate	1706007	23549	40	20170720*
Euro OTC	Magnesium citrate	1711018	23895	40	20171129*
Euro OTC	Magnesium citrate	1803033	24088	40	20180403*
Euro OTC	Magnesium citrate	1808020	24202	40	20180827*
Euro OTC	Magnesium citrate	1902006	24480	40	20190226*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 480 spectra of 10 reference samples from the substance/substance group *Magnesium citrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 209 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 160 spectra of 4 reference samples from the substance/substance group *Magnesium citrate*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Magnesium citrate	1607006	22673	40
Euro OTC	Magnesium citrate	1701018	22998	40
Euro OTC	Magnesium citrate	1810026	24308	40
Euro OTC	Magnesium citrate	1907040	24778	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Magnesium citrate*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
APOrtha Deutschland GmbH	Magnesium citrate	17000809/0	1
Arktis	Magnesium citrate	894P/2418	1
Euro OTC	Magnesium citrate	1602028-01	1
Euro OTC	Magnesium citrate	1808020-01	1
Euro OTC	Magnesium citrate	1706007-01	2

- 111 241 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Magnesium citrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium citrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	480	0	110 209
Type B	0	125	35	118 982
Type C	0	6	0	111 241

The substance/substance group *Magnesium citrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7500 %)
Type B	100.0000 % (> 99.9893 %)	78.1250 % (> 76.2500 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium citrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Riboflavin phosphate sodium	18.87	—
Levothyroxin sodium	29.53	—
Calcium citrate tetrahydrate	36.38	—
Polymyxin B sulfate	44.43	—
Minoxidil	46.48	—
L-glutathione	49.37	—
Bacitracin	50.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium citrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22505	22505	0.00	26.31
23895	23895	0.00	28.93
21860	21860	0.00	24.16
24088	24088	0.00	29.69
21794	21794	0.00	29.89
21829	21829	0.00	27.73
24202	24202	0.00	31.17

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22225	22225	0.00	32.46
24480	24480	0.00	29.94
23549	23549	0.00	27.25

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Magnesium hydrogen aspartate tetrahydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20812-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnesium hydrogen aspartate tetrahydrate; Magnesii asparticum tetrahydricum

Special notes

When selecting the *Magnesium hydrogen aspartate tetrahydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Magnesium hydrogen aspartate tetrahydrate	6	2	1

Second-stage model

For differentiation of the substance/substance group *Magnesium hydrogen aspartate tetrahydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium hydrogen aspartate tetrahydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Magnesium hydrog...	1204014-01	20812	40	1404588
Euro OTC	Magnesium hydrog...	1306045-01	21749	60	20130708
Euro OTC	Magnesium hydrog...	1605031	22682	40	20160617*
Euro OTC	Magnesium hydrog...	1901036	24488	40	20190227*
Euro OTC	Magnesium hydrog...	1906029	24773	40	20190712*
Euro OTC	Magnesium hydrog...	2002039	25125	40	20200331*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Magnesium hydrogen aspartate tetrahydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Magnesium hydrogen aspartate tetrahydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Magnesium hydrogen aspartate...	1707010	23552	40
Euro OTC	Magnesium hydrogen aspartate...	1806011	24156	40
Euro OTC	Magnesium hydrogen aspartate...	1707010	23608	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Magnesium hydrogen aspartate tetrahydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Magnesium hydrogen aspartate...	1605031-01	1

- 111 246 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Magnesium hydrogen aspartate tetrahydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium hydrogen aspartate tetrahydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	1	0	111 246

The substance/substance group *Magnesium hydrogen aspartate tetrahydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8911 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium hydrogen aspartate tetrahydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	53.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium hydrogen aspartate tetrahydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22682	22682	0.00	53.60
20812	20812	0.00	52.36
21749	20812	4.64	54.05
24488	24488	0.00	53.43
24773	24773	0.00	52.99
25125	25125	0.00	52.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Magnesium hydrogen citrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20016-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnesium hydrogen citrate; Magnesii hydrogenocitras hydricus; Magnesium hydrogen citrate, hydrated

Special notes

When selecting the *Magnesium hydrogen citrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Magnesium hydrogen citrate	6	14	174

Second-stage model

For differentiation of the substance/substance group *Magnesium hydrogen citrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium hydrogen citrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Magnesium hydrog...	13389102	21445	60	20131205
Caelo	Magnesium hydrog...	15415014	23240	40	20160105
Euro OTC	Magnesium hydrog...	1507010	21873	60	20150713*
Euro OTC	Magnesium hydrog...	1510033	22233	60	20151117*
Euro OTC	Magnesium hydrog...	1601005	22296	60	20160119*
Euro OTC	Magnesium hydrog...	1701003	22992	40	20170124*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Magnesium hydrogen citrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 369 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 560 spectra of 14 reference samples from the substance/substance group *Magnesium hydrogen citrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Magnesium hydrogen citrate	173531	23788	40
Caelo	Magnesium hydrogen citrate	182746	24397	40
Euro OTC	Magnesium hydrogen citrate	1604002	22509	40
Euro OTC	Magnesium hydrogen citrate	1608004	22796	40
Euro OTC	Magnesium hydrogen citrate	1701004	22991	40
Euro OTC	Magnesium hydrogen citrate	1705010	23380	40
Euro OTC	Magnesium hydrogen citrate	1705009	23382	40
Euro OTC	Magnesium hydrogen citrate	1710007	23771	40
Euro OTC	Magnesium hydrogen citrate	1802026	24064	40
Euro OTC	Magnesium hydrogen citrate	1811038	24425	40
Euro OTC	Magnesium hydrogen citrate	1904011	24620	40
Euro OTC	Magnesium hydrogen citrate	1907020	24777	40
Euro OTC	Magnesium hydrogen citrate	1910005	24934	40
Fagron	Magnesium hydrogen citrate	19I23-B02-195296	24953	40

- 118 582 spectra from a total of 2406 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 546 spectra from 188 *Apo-Ident* customers from 178 batches from the substance/substance group *Magnesium hydrogen citrate*.
- Among them are spectra of independent samples from 172 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
/Sanacorp	Magnesium hydrogen citrate	90170	1
ACM	Magnesium hydrogen citrate	KNC0829J15	1
ACM	Magnesium hydrogen citrate	KNC1377J15	2
AHD	Magnesium hydrogen citrate	13389103	1
Fagron	Magnesium hydrogen citrate	15296701	1
Alliance health	Magnesium hydrogen citrate	13389111	2
Anzag	Magnesium hydrogen citrate	16341710	1
Bombastus	Magnesium hydrogen citrate	1608004-01	1
Caelo	Magnesium hydrogen citrate	12175807	3
Caelo	Magnesium hydrogen citrate	11372901	1
Caelo	Magnesium hydrogen citrate	13389106	2
Caelo	Magnesium hydrogen citrate	14265505	2
Caelo	Magnesium hydrogen citrate	1214	1
Caelo	Magnesium hydrogen citrate	12175801	1
Caelo	Magnesium hydrogen citrate	12175802	2
Caelo	Magnesium hydrogen citrate	26101203	1
Caelo	Magnesium hydrogen citrate	12175810	5
Caelo	Magnesium hydrogen citrate	12238002	3
Caelo	Magnesium hydrogen citrate	12238012	1

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Supplier	Substance	Batch	Spectra
Caelo	Magnesium hydrogen citrate	12238004	3
Caelo	Magnesium hydrogen citrate	12368003	9
Caelo	Magnesium hydrogen citrate	12368004	2
Caelo	Magnesium hydrogen citrate	11193104	1
Caelo	Magnesium hydrogen citrate	19061316	1
Caelo	Magnesium hydrogen citrate	12368011	8
Caelo	Magnesium hydrogen citrate	80446188	1
Caelo	Magnesium hydrogen citrate	2368011	1
Caelo	Magnesium hydrogen citrate	12368002	3
Caelo	Magnesium hydrogen citrate	6081301	1
Caelo	Magnesium hydrogen citrate	12368017	2
Caelo	Magnesium hydrogen citrate	12091303	1
Caelo	Magnesium hydrogen citrate	13194601	4
Caelo	Magnesium hydrogen citrate	13233904	5
Caelo	Magnesium hydrogen citrate	27111306	1
Caelo	Magnesium hydrogen citrate	13233905	1
Caelo	Magnesium hydrogen citrate	13233911	3
Caelo	Magnesium hydrogen citrate	411052-2-P	1
Caelo	Magnesium hydrogen citrate	11021401	1
Caelo	Magnesium hydrogen citrate	13389103	7
Caelo	Magnesium hydrogen citrate	11061403	1
Caelo	Magnesium hydrogen citrate	17061401	1
Caelo	Magnesium hydrogen citrate	13233913	6
Caelo	Magnesium hydrogen citrate	13233910	5
Caelo	Magnesium hydrogen citrate	13389111	4
Caelo	Magnesium hydrogen citrate	133389111	1
Caelo	Magnesium hydrogen citrate	7011504	1
Caelo	Magnesium hydrogen citrate	14265511	1
Caelo	Magnesium hydrogen citrate	14265504	5
Caelo	Magnesium hydrogen citrate	14265514	1
Caelo	Magnesium hydrogen citrate	14265513	2
Caelo	Magnesium hydrogen citrate	13389108	1
Caelo	Magnesium hydrogen citrate	14265521	1
Caelo	Magnesium hydrogen citrate	14265516	3
Caelo	Magnesium hydrogen citrate	15296712	2
Caelo	Magnesium hydrogen citrate	15415001	6
Caelo	Magnesium hydrogen citrate	1604002-01	3
Caelo	Magnesium hydrogen citrate	160100501	1
Caelo	Magnesium hydrogen citrate	15415004	2
Caelo	Magnesium hydrogen citrate	14265520	1
Caelo	Magnesium hydrogen citrate	16341711	2
Caelo	Magnesium hydrogen citrate	16341710	6
Caelo	Magnesium hydrogen citrate	27101704	1
Caelo	Magnesium hydrogen citrate	17173404	1
Caelo	Magnesium hydrogen citrate	17353104	2
Caelo	Magnesium hydrogen citrate	18216803	3
Caelo	Magnesium hydrogen citrate	1904011-01	2
Caelo	Magnesium hydrogen citrate	18274604	1
Caelo	Magnesium hydrogen citrate	11372902	1
Caelo	Magnesium hydrogen citrate	15415013	2
Caelo	Magnesium hydrogen citrate	13389107	2
Caelo	Magnesium hydrogen citrate	14265517	1
Caelo	Magnesium hydrogen citrate	15296801	3
Caelo	Magnesium hydrogen citrate	15415002	1
Caelo	Magnesium hydrogen citrate	15415005	3
Caelo	Magnesium hydrogen citrate	12368014	2
Caelo	Magnesium hydrogen citrate	17173405	3
Caelo	Magnesium hydrogen citrate	13233901	7
Caelo	Magnesium hydrogen citrate	913M-01829	1
Caelo	Magnesium hydrogen citrate	1014E-01829	1

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Supplier	Substance	Batch	Spectra
Caelo	Magnesium hydrogen citrate	315E-01829	1
Caelo	Magnesium hydrogen citrate	516Q-01829	1
Caelo	Magnesium hydrogen citrate	12368005	1
Caelo	Magnesium hydrogen citrate	15415009	5
Caelo	Magnesium hydrogen citrate	16341709	2
Caelo	Magnesium hydrogen citrate	1710007-01	2
Caelo	Magnesium hydrogen citrate	133233907	1
Caelo	Magnesium hydrogen citrate	1601005-01	1
Caelo	Magnesium hydrogen citrate	121033-01	1
Caelo	Magnesium hydrogen citrate	13233907	2
Caelo	Magnesium hydrogen citrate	15296701	7
Caelo	Magnesium hydrogen citrate	16341707	1
Caelo	Magnesium hydrogen citrate	16341708	4
Caelo	Magnesium hydrogen citrate	1507010-01	2
Caelo	Magnesium hydrogen citrate	11044103	2
Caelo	Magnesium hydrogen citrate	15415015	1
Caelo	Magnesium hydrogen citrate	17173401	3
Caelo	Magnesium hydrogen citrate	90396169	1
Caelo	Magnesium hydrogen citrate	14265503	6
Caelo	Magnesium hydrogen citrate	15296709	4
Caelo	Magnesium hydrogen citrate	15296710	1
Caelo	Magnesium hydrogen citrate	16E02-B03-321485	1
Caelo	Magnesium hydrogen citrate	15415010	9
Caelo	Magnesium hydrogen citrate	17173406	1
Caelo	Magnesium hydrogen citrate	14I12-B02-298854	1
Caelo	Magnesium hydrogen citrate	15296702	4
Caelo	Magnesium hydrogen citrate	1415013	1
Caelo	Magnesium hydrogen citrate	18274602	1
Caelo	Magnesium hydrogen citrate	13194603	1
Caelo	Magnesium hydrogen citrate	15415003	6
Caeolo/Gehe	Magnesium hydrogen citrate	17173405	2
Cealo	Magnesium hydrogen citrate	12368014	1
Cealo	Magnesium hydrogen citrate	13233907	2
Dr. Paul Lohmann	Magnesium hydrogen citrate	1078434	1
Dr. Paul Lohmann	Magnesium hydrogen citrate	1079474	1
Dr. Paul Lohmann	Magnesium hydrogen citrate	1077866	2
Eu Rho	Magnesium hydrogen citrate	110600401	1
Eu Rho	Magnesium hydrogen citrate	1202034-01	1
Eu Rho	Magnesium hydrogen citrate	1306034-01	1
EuRho	Magnesium hydrogen citrate	1311003-02	1
EuRho/Phönix	Magnesium hydrogen citrate	1202034-02	1
EuRho/Phönix	Magnesium hydrogen citrate	1311003-01	1
Euro OTC	Magnesium hydrogen citrate	1306034-02	2
Euro OTC	Magnesium hydrogen citrate	140402301	1
Euro OTC	Magnesium hydrogen citrate	1085730	2
Euro OTC	Magnesium hydrogen citrate	1507010-01	10
Euro OTC	Magnesium hydrogen citrate	1510033-01	2
Euro OTC	Magnesium hydrogen citrate	160100501	1
Euro OTC	Magnesium hydrogen citrate	1601005-01	13
Euro OTC	Magnesium hydrogen citrate	16000456/0	1
Euro OTC	Magnesium hydrogen citrate	1604002-02	8
Euro OTC	Magnesium hydrogen citrate	1608004-01	22
Euro OTC	Magnesium hydrogen citrate	160800401	2
Euro OTC	Magnesium hydrogen citrate	1701004-01	4
Euro OTC	Magnesium hydrogen citrate	1710007-01	9
Euro OTC	Magnesium hydrogen citrate	1608004-02	2
Euro OTC	Magnesium hydrogen citrate	1710001-01	1
Euro OTC	Magnesium hydrogen citrate	1404023-01	5
Euro OTC	Magnesium hydrogen citrate	1604002-001	1
Euro OTC	Magnesium hydrogen citrate	1211033-01	4

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Supplier	Substance	Batch	Spectra
Euro OTC	Magnesium hydrogen citrate	130603402	1
Euro OTC	Magnesium hydrogen citrate	1701003-01	7
Euro OTC	Magnesium hydrogen citrate	1311003-02	1
Euro OTC	Magnesium hydrogen citrate	2114M1829	1
Euro OTC	Magnesium hydrogen citrate	1802026-01	5
Euro OTC	Magnesium hydrogen citrate	1808006-01	3
Euro OTC	Magnesium hydrogen citrate	1407048-01	4
Euro OTC	Magnesium hydrogen citrate	140704801	1
Euro OTC	Magnesium hydrogen citrate	120800602	1
Euro OTC	Magnesium hydrogen citrate	1604002-012x	1
Euro OTC	Magnesium hydrogen citrate	1110026-01	2
Euro OTC	Magnesium hydrogen citrate	1705009-01	5
Euro OTC	Magnesium hydrogen citrate	1208006-01	3
Euro OTC	Magnesium hydrogen citrate	1211033-02	4
Euro OTC	Magnesium hydrogen citrate	1501026-01	5
Euro OTC	Magnesium hydrogen citrate	1507010-02	2
Euro OTC	Magnesium hydrogen citrate	190401101	1
Euro OTC	Magnesium hydrogen citrate	1705010-01	5
Euro OTC	Magnesium hydrogen citrate	1811038-01	6
Euro OTC	Magnesium hydrogen citrate	1080144	1
Euro OTC	Magnesium hydrogen citrate	1407048-02	3
Fagron	Magnesium hydrogen citrate	12G10-N01	2
Fagron	Magnesium hydrogen citrate	1056239	1
Fagron	Magnesium hydrogen citrate	13D30-N07	2
Fagron	Magnesium hydrogen citrate	14/12-B02-298854	1
Fagron	Magnesium hydrogen citrate	3047166	2
Fagron	Magnesium hydrogen citrate	11H05-N07	1
Fagron	Magnesium hydrogen citrate	14I12-B02-298854	1
Fagron	Magnesium hydrogen citrate	13B22-N03	1
Fagron	Magnesium hydrogen citrate	17G24-B03-341019	1
Fagron	Magnesium hydrogen citrate	14K-B03-305254	1
Fagron	Magnesium hydrogen citrate	13K11-B02-288161	1
Fagron	Magnesium hydrogen citrate	18I20-B06-355658	1
Fagron	Magnesium hydrogen citrate	13233901	2
Fagron	Magnesium hydrogen citrate	13K11-B02-288161	1
Fagron	Magnesium hydrogen citrate	14I12-B02	1
Fagron	Magnesium hydrogen citrate	16E02-B03-0326874	1
Fagron	Magnesium hydrogen citrate	16E02-B03-326874	1
Fiebig	Magnesium hydrogen citrate	1802026-01	1
Gatt-Koller	Magnesium hydrogen citrate	1802721	1
Gatt-Koller	Magnesium hydrogen citrate	1803714	2
Gatt-Koller	Magnesium hydrogen citrate	1800208	1
Gehe Kassel	Magnesium hydrogen citrate	14/12-B02-298854	1
Heidelberger Chlorella	Magnesium hydrogen citrate	90196	1
Heidelberger Chlorella/...	Magnesium hydrogen citrate	10032	1
Ichthyol/Phönix	Magnesium hydrogen citrate	14/12-B02-298854	1
Kehr	Magnesium hydrogen citrate	17173406	1
kögl	Magnesium hydrogen citrate	1900910	1
L30	Magnesium hydrogen citrate	1608004-01	1
lohmann	Magnesium hydrogen citrate	3054132	1
Nachprüfung vom 31.12.2...	Magnesium hydrogen citrate	16341710	1
Nowed18.08.2015	Magnesium hydrogen citrate	14265521	1
Noweda	Magnesium hydrogen citrate	10163306	1
Noweda	Magnesium hydrogen citrate	16341710	1
Euro OTC	Magnesium hydrogen citrate	1604002-01	32
Phoenix 15.10.14	Magnesium hydrogen citrate	1311003-01	1
Euro OTC	Magnesium hydrogen citrate	1904011-01	5
phönix	Magnesium hydrogen citrate	1601005-01	2
phönix	Magnesium hydrogen citrate	15296702	1
phönix	Magnesium hydrogen citrate	1604002-01	1

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Supplier	Substance	Batch	Spectra
phönix	Magnesium hydrogen citrate	15296710	1
phönix	Magnesium hydrogen citrate	15415010	1
phönix	Magnesium hydrogen citrate	15415015	2
phönix	Magnesium hydrogen citrate	16341709	2
phönix	Magnesium hydrogen citrate	1608004-01	1
Phönix	Magnesium hydrogen citrate	1211033-01	2
Phönix	Magnesium hydrogen citrate	15415005	1
Euro OTC	Magnesium hydrogen citrate	151003301	2
Sanacaorp	Magnesium hydrogen citrate	13389108	1
Caelo	Magnesium hydrogen citrate	13233906	9
Euro OTC	Magnesium hydrogen citrate	1306034-01	2
Euro OTC	Magnesium hydrogen citrate	1311003-01	7
VDL;27.02.15	Magnesium hydrogen citrate	13389111	1
	Magnesium hydrogen citrate	1311003-01	1
Caelo	Magnesium hydrogen citrate		1
Caelo	Magnesium hydrogen citrate	15415014	5
	Magnesium hydrogen citrate	1510033-01	1
Euro OTC	Magnesium hydrogen citrate		2
Fagron	Magnesium hydrogen citrate		1
Gatt-Koller	Magnesium hydrogen citrate		1

- 110 701 spectra from 742 *Apo-Ident* customers from a total of 31 717 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Magnesium hydrogen citrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium hydrogen citrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	560	0	118 582
Type C	0	537	9	110 701

The substance/substance group *Magnesium hydrogen citrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.9286 %)
Type C	100.0000 % (> 99.8899 %)	98.3516 % (> 97.8022 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium hydrogen citrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Gentamicin sulfate	19.17	—
Magnesium citrate	31.09	—
Riboflavin phosphate sodium	40.64	—
Levothyroxin sodium	40.92	—
Calcium colamine phosphate	46.01	—
Menthol	56.97	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium hydrogen citrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21873	21873	0.00	19.20
22233	22233	0.00	19.17
22296	22296	0.00	19.73
22992	22992	0.00	20.36
21445	22233	3.33	19.27
23240	22992	2.73	20.55

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Magnesium orotate dihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20429-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnesium orotate dihydrate; Magnesii oroticum dihydricum

Special notes

When selecting the *Magnesium orotate dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Magnesium orotate dihydrate	5	9	21

Second-stage model

For differentiation of the substance/substance group *Magnesium orotate dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium orotate dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Magnesium orotat...	162227	22638	40	20160809*
Caelo	Magnesium orotat...	16222701	23236	40	20160809
Euro OTC	Magnesium orotat...	1511021	22287	60	20151228*
Euro OTC	Magnesium orotat...	1707018	23615	40	20170907*
Euro OTC	Magnesium orotat...	1911024	25069	40	20200107*

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Magnesium orotate dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Magnesium orotate dihydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Magnesium orotate dihydrate	172157	23661	40
Caelo	Magnesium orotate dihydrate	172547	23799	40
Euro OTC	Magnesium orotate dihydrate	1608017	22784	40
Euro OTC	Magnesium orotate dihydrate	1712001	23874	40
Euro OTC	Magnesium orotate dihydrate	1802018	23963	40
Euro OTC	Magnesium orotate dihydrate	1808029	24200	40
Euro OTC	Magnesium orotate dihydrate	1902007	24490	40
Euro OTC	Magnesium orotate dihydrate	1906014	24797	40
Euro OTC	Magnesium orotate dihydrate	1909007	24835	40

- 118 782 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 38 spectra from 18 *Apo-Ident* customers from 21 batches from the substance/substance group *Magnesium orotate dihydrate*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Magnesium orotate dihydrate	14093607	2
Euro OTC	Magnesium orotate dihydrate	1712001-01	2
Euro OTC	Magnesium orotate dihydrate	151102101	1
Euro OTC	Magnesium orotate dihydrate	1707018-01	3
Euro OTC	Magnesium orotate dihydrate	1305011-01	1
Euro OTC	Magnesium orotate dihydrate	1504002-01	1
Euro OTC	Magnesium orotate dihydrate	1802018-01	1
Euro OTC	Magnesium orotate dihydrate	1209029-01	3
Euro OTC	Magnesium orotate dihydrate	1608017-01	2
Euro OTC	Magnesium orotate dihydrate	16085017-01	1
Euro OTC	Magnesium orotate dihydrate	1305011-02	5
Euro OTC	Magnesium orotate dihydrate	1511021-02	6
Fagron	Magnesium orotate dihydrate	1000060461	1
Fagron	Magnesium orotate dihydrate	13H06-N07	1
Fagron	Magnesium orotate dihydrate	12G05-N03	1
Fagron	Magnesium orotate dihydrate	160801701	1
Fagron	Magnesium orotate dihydrate	16K22B01329783	1
Fagron	Magnesium orotate dihydrate	14/13-B05-305616	1
Fagron	Magnesium orotate dihydrate	14E20-B05-296005	1
Euro OTC	Magnesium orotate dihydrate	1407005-01	2
Euro OTC	Magnesium orotate dihydrate	130501102	1

- 111 209 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Magnesium orotate dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium orotate dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	360	0	118 782
Type C	0	37	1	111 209

The substance/substance group *Magnesium orotate dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8899 %)	97.3684 % (> 89.4737 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium orotate dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Manganese orotate dihydrate	29.77	–
Aciclovir	67.68	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium orotate dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22287	22287	0.00	49.21
22638	22638	0.00	64.61
23236	22638	3.64	61.48
23615	23615	0.00	56.00
25069	25069	0.00	61.78

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Magnesium stearate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20707-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Magnesium stearate; Magnesii stearas

Special notes

When selecting the *Magnesium stearate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Magnesium stearate	6	6	20

Second-stage model

For differentiation of the substance/substance group *Magnesium stearate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Magnesium stearate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Magnesium stearate	13095536	21117	40	20130405
Caelo	Magnesium stearate	14136929	21783	60	AR-15-FG-012028-01
Euro OTC	Magnesium stearate	1502033-01	22817	40	20150317
Euro OTC	Magnesium stearate	1704002	23436	40	20170622*
Fagron	Magnesium stearate	12C29-N06	20707	110	20120418
Fagron	Magnesium stearate	12D26-B03	21084	40	1407310

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 330 spectra of 6 reference samples from the substance/substance group *Magnesium stearate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 359 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Magnesium stearate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Magnesium stearate	162066	22763	40
Caelo	Magnesium stearate	181533	24215	40
Caelo	Magnesium stearate	183089	24354	40
Caelo	Magnesium stearate	192527	24897	40
Euro OTC	Magnesium stearate	1608022	22821	40
Euro OTC	Magnesium stearate	1901033	24459	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 29 spectra from 20 *Apo-Ident* customers from 21 batches from the substance/substance group *Magnesium stearate*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Magnesium stearate	15305302	3
Caelo	Magnesium stearate	16206617	1
Caelo	Magnesium stearate	18308916	1
Caelo	Magnesium stearate	16206602	3
Caelo	Magnesium stearate	16206610	2
Caelo	Magnesium stearate	15305307	1
Caelo	Magnesium stearate	15305315	3
Caelo	Magnesium stearate	18308912	1
Caelo	Magnesium stearate	12040307	1
Caelo	Magnesium stearate	13095515	1
Caelo	Magnesium stearate	15155001	2
Caelo	Magnesium stearate	183038912	1
Caelo	Magnesium stearate	15305323	1
Caesar & Loretz GmbH / ...	Magnesium stearate	15322002	1
Euro OTC	Magnesium stearate	1912I-01834	1
Euro OTC	Magnesium stearate	914I-01834	1
Euro OTC	Magnesium stearate	315E-01834	1
Euro OTC	Magnesium stearate	1116E-01834	1
Fagron	Magnesium stearate	12D26-B03-289435	1
Caelo	Magnesium stearate	17360006	1
Caelo	Magnesium stearate	13095536	1

- 111 218 spectra from 742 *Apo-Ident* customers from a total of 31 870 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Magnesium stearate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Magnesium stearate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	330	0	110 359
Type B	0	240	0	118 902
Type C	0	26	3	111 218

The substance/substance group *Magnesium stearate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1818 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	89.6552 % (> 79.3103 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Magnesium stearate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Wax, bleached	36.21	—
Cocoa butter	37.36	—
Hard fat in pastilles	42.85	—
Hard fat W35	47.91	—
Sodium dodecyl sulfate	49.18	—
Paraffin, microcrystalline	49.58	—
Cetyl palmitate 15	51.54	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Magnesium stearate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21117	21084	23.75	77.23
21084	21084	0.00	53.10
23436	23436	0.00	59.42
20707	21084	12.87	39.45
21783	21783	0.00	33.38
22817	21783	4.15	36.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Manganese orotate dihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22311-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Manganese orotate dihydrate

Special notes

When selecting the *Manganese orotate dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Manganese orotate dihydrate	3	1	0

Second-stage model

For differentiation of the substance/substance group *Manganese orotate dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Manganese orotate dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Manganese orotat...	1601003	22311	60	20160113*
Euro OTC	Manganese orotat...	1801031	23908	40	20180131*
Euro OTC	Manganese orotat...	1907009	24787	40	20190718*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Manganese orotate dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Manganese orotate dihydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Manganese orotate dihydrate	1605029-01	22654	40
Euro OTC	Manganese orotate dihydrate	1605029-01	22737	40

- 119062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Manganese orotate dihydrate*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Manganese orotate dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Manganese orotate dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	0	0	111 247

The substance/substance group *Manganese orotate dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Manganese orotate dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium orotate dihydrate	19.87	—
Aciclovir	54.99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Manganese orotate dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22311	22311	0.00	46.55
23908	23908	0.00	40.28
24787	24787	0.00	42.38

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Mannitol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20118-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mannitol; Mannitolum

Special notes

When selecting the *Mannitol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mannitol	6	22	436

Second-stage model

For differentiation of the substance/substance group *Mannitol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mannitol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Mannitol	12305723	20980	40	1402329
Caelo	Mannitol	15197305	22581	40	20150720
Euro OTC	Mannitol	1508012	21884	60	20150827*
Euro OTC	Mannitol	1511025	22286	60	20151228*
Fagron	Mannitol	15A26-B01-305841	22883	40	20150204
Fagron	Mannitol	15A26-B01-305841	22884	40	20150204
Fagron	Mannitol	17B08-B04-352402	24579	40	20170517

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 7 reference samples from the substance/substance group *Mannitol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 369 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1010 spectra of 25 reference samples from the substance/substance group *Mannitol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Mannitol	160140	22458	60
Caelo	Mannitol	16014013	22580	40
Caelo	Mannitol	162009	22614	40
Caelo	Mannitol	162121	22721	40
Caelo	Mannitol	170879	23296	40
Caelo	Mannitol	170450	23318	40
Caelo	Mannitol	172588	23800	40
Caelo	Mannitol	182654	24368	40
Caelo	Mannitol	182655	24385	40
Caelo	Mannitol	191654	24723	40
Euro OTC	Mannitol	1604008	22515	40
Euro OTC	Mannitol	1606031	22697	40
Euro OTC	Mannitol	1610027	22862	40
Euro OTC	Mannitol	1703043	23125	40
Euro OTC	Mannitol	1708005	23700	40
Euro OTC	Mannitol	1802004	23966	40
Euro OTC	Mannitol	1806024	24152	40
Euro OTC	Mannitol	1809008	24327	40
Euro OTC	Mannitol	1902011	24476	40
Euro OTC	Mannitol	1904025	24600	40
Euro OTC	Mannitol	1908019	24857	40
Fagron	Mannitol	18H16-B01	24817	40
Caelo	Mannitol	162121	23066	30
Caelo	Mannitol	160140	23299	40
Caelo	Mannitol	170879	23305	40

- 118 132 spectra from a total of 2398 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1558 spectra from 410 *Apo-Ident* customers from 438 batches from the substance/substance group *Mannitol*.
- Among them are spectra of independent samples from 435 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Mannitol	1230578	1
Caelo	Mannitol	1610027-01	3
ALH	Mannitol	1409016-01	1
ALH	Mannitol	1703043-01	1
ALH/EuRho	Mannitol	1802004-01	1
Alliance Health 12.08.2...	Mannitol	1404034-01	2
allianz	Mannitol	16212101	2
Allianz Healthcare 26.0...	Mannitol	1502022-01	1

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Supplier	Substance	Batch	Spectra
Anzag	Mannitol	1310004-02	1
ANZAG	Mannitol	1211034-01	1
Apo Ident/ Noweda	Mannitol	1610027-01	1
ApoIdent/Noweda	Mannitol	1610027-01	1
apomix	Mannitol	1708005-01	2
Apomix	Mannitol	1310004-01	1
Bombastus	Mannitol	16340301	1
Cael Sanacorp 05.02.2016	Mannitol	14323138	2
Caelo	Mannitol	11219121	1
Caelo	Mannitol	13189203	8
Caelo	Mannitol	15184101	1
Caelo	Mannitol	16H25-B03-326639	1
Caelo	Mannitol	1110009-02	1
Caelo	Mannitol	12105405	1
Caelo	Mannitol	11219124	2
Caelo	Mannitol	12105403	3
Caelo	Mannitol	12105404	3
Caelo	Mannitol	12105421	9
Caelo	Mannitol	11219122	1
Caelo	Mannitol	11D01-N10	1
Caelo	Mannitol	20151012-2	1
Caelo	Mannitol	12105438	2
Caelo	Mannitol	9204719	1
Caelo	Mannitol	10100026	2
Caelo	Mannitol	5031304	1
Caelo	Mannitol	12305710	8
Caelo	Mannitol	1211034-01	1
Caelo	Mannitol	9081303	1
Caelo	Mannitol	12305725	11
Caelo	Mannitol	23082013C	1
Caelo	Mannitol	12305724	5
Caelo	Mannitol	12305726	1
Caelo	Mannitol	12305734	2
Caelo	Mannitol	24101306	1
Caelo	Mannitol	13189201	8
Caelo	Mannitol	13189206	1
Caelo	Mannitol	16011402	1
Caelo	Mannitol	1305043-02	3
Caelo	Mannitol	12305728	2
Caelo	Mannitol	13189226	4
Caelo	Mannitol	16061401	1
Caelo	Mannitol	13189222	3
Caelo	Mannitol	7071404	1
Caelo	Mannitol	14051204	8
Caelo	Mannitol	13189227	11
Caelo	Mannitol	14051207	1
Caelo	Mannitol	14051205	6
Caelo	Mannitol	2101401	1
Caelo	Mannitol	14051215	5
Caelo	Mannitol	14051208	2
Caelo	Mannitol	13K20-B01-287704	1
Caelo	Mannitol	1405127	1
Caelo	Mannitol	14051217	2
Caelo	Mannitol	14051224	2
Caelo	Mannitol	30121417	1
Caelo	Mannitol	10011501	1
Caelo	Mannitol	14051223	1
Caelo	Mannitol	14051216	3
Caelo	Mannitol	14051230	2
Caelo	Mannitol	14323101	3

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Supplier	Substance	Batch	Spectra
Caelo	Mannitol	14051229	5
Caelo	Mannitol	30031502	1
Caelo	Mannitol	14323105	2
Caelo	Mannitol	14323115	4
Caelo	Mannitol	1502022-01	1
Caelo	Mannitol	1423120	1
Caelo	Mannitol	14323127	4
Caelo	Mannitol	14323120	1
Caelo	Mannitol	14323125	2
Caelo	Mannitol	14323129	1
Caelo	Mannitol	8720	1
Caelo	Mannitol	15197303	1
Caelo	Mannitol	15197302	5
Caelo	Mannitol	1508012-02	1
Caelo	Mannitol	2274635	1
Caelo	Mannitol	48558	1
Caelo	Mannitol	15525	1
Caelo	Mannitol	15197314	6
Caelo	Mannitol	16D20-B03	1
Caelo	Mannitol	15197312	1
Caelo	Mannitol	15197327	1
Caelo	Mannitol	16212103	1
Caelo	Mannitol	160400801	1
Caelo	Mannitol	162121	1
Caelo	Mannitol	15197219	1
Caelo	Mannitol	16014005	11
Caelo	Mannitol	16212109	4
Caelo	Mannitol	8031704	1
Caelo	Mannitol	16340302	7
Caelo	Mannitol	16200903	10
Caelo	Mannitol	1606031-02	1
Caelo	Mannitol	16200913	4
Caelo	Mannitol	17A12-B03	1
Caelo	Mannitol	17045001	3
Caelo	Mannitol	17045003	9
Caelo	Mannitol	1071701	1
Caelo	Mannitol	16200912	4
Caelo	Mannitol	1610018-01	1
Caelo	Mannitol	163403	1
Caelo	Mannitol	17045004	2
Caelo	Mannitol	16200924	8
Caelo	Mannitol	151117	1
Caelo	Mannitol	4516E-01844	1
Caelo	Mannitol	18121701	1
Caelo	Mannitol	17087908	9
Caelo	Mannitol	17045006	2
Caelo	Mannitol	17045009	12
Caelo	Mannitol	17I13-B02-340966	1
Caelo	Mannitol	17045010	5
Caelo	Mannitol	17045008	7
Caelo	Mannitol	17087907	1
Caelo	Mannitol	17J30-B10-3434414	1
Caelo	Mannitol	9061808	1
Caelo	Mannitol	17360110	3
Caelo	Mannitol	1708005-01	1
Caelo	Mannitol	27101802	1
Caelo	Mannitol	18D09-B13-352214	1
Caelo	Mannitol	18D09-B12-351437	1
Caelo	Mannitol	18265502	7
Caelo	Mannitol	17258819	4

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Supplier	Substance	Batch	Spectra
Caelo	Mannitol	17258831	1
Caelo	Mannitol	18265506	6
Caelo	Mannitol	13189228	1
Caelo	Mannitol	16014014	1
Caelo	Mannitol	170800501	3
Caelo	Mannitol	16212102	10
Caelo	Mannitol	13095013	1
Caelo	Mannitol	16340301	12
Caelo	Mannitol	16200908	2
Caelo	Mannitol	17045002	16
Caelo	Mannitol	15197319	7
Caelo	Mannitol	17360108	11
Caelo	Mannitol	14323124	2
Caelo	Mannitol	14051209	7
Caelo	Mannitol	1400434-01	1
Caelo	Mannitol	1409016-01	1
Caelo	Mannitol	16014013	1
Caelo	Mannitol	1205016-02	2
Caelo	Mannitol	17258808	5
Caelo	Mannitol	17258820	2
Caelo	Mannitol	15K25-B04	1
Caelo	Mannitol	17258830	1
Caelo	Mannitol	1612101	1
Caelo	Mannitol	16014016	1
Caelo	Mannitol	170450	1
Caelo	Mannitol	19165401	1
Caelo	Mannitol	14323138	23
Caelo	Mannitol	17087915	1
Caelo	Mannitol	14323103	2
Caelo	Mannitol	13189207	8
Caelo	Mannitol	12305725-3444311112	1
Caelo	Mannitol	1404034-01	2
Caelo	Mannitol	16G27-B03	1
Caelo	Mannitol	13189208	6
Caelo	Mannitol	14323114	3
Caelo	Mannitol	16212104	2
Caelo	Mannitol	17258812	3
Caelo	Mannitol	1809008-01	3
Caelo	Mannitol	11(16200912)	1
Caelo	Mannitol	18265428	2
Caelo	Mannitol	16200901	2
Caelo	Mannitol	12305740	2
Caelo	Mannitol	1508012-01	2
Caelo	Mannitol	1621212	1
Caelo	Mannitol	16200904	2
Caelo	Mannitol	15197329	1
Caelo	Mannitol	16236603	1
Caelo	Mannitol	17087916	15
Caelo	Mannitol	200218P302	1
Caelo	Mannitol	180602401	1
Caelo	Mannitol	18b23-b09	1
Caelo	Mannitol	12305709	16
Caelo	Mannitol	16212101	11
Caelo	Mannitol	17360101	11
Caelo	Mannitol	17360115	3
Caelo	Mannitol	18265507	1
Caelo	Mannitol	13189215	17
Caelo	Mannitol	4414E-01844	1
Caelo	Mannitol	15D28-B02-309192	4
Caelo	Mannitol	16212106	4

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Supplier	Substance	Batch	Spectra
Caelo	Mannitol	17087909	1
Caelo	Mannitol	E911K	1
Caelo	Mannitol	17360112	7
Caelo	Mannitol	18265411	2
Caelo	Mannitol	18265505	1
Caelo	Mannitol	12105420	7
Caelo	Mannitol	11003611	1
Caelo	Mannitol	11308807	2
Caelo	Mannitol	13189203-3566412081	1
Caelo	Mannitol	14323121	6
Caelo	Mannitol	14323126	4
Caelo	Mannitol	1519713	1
Caelo	Mannitol	18265504	3
Caesar	Mannitol	1508012-1	1
Caesar & Loretz GmbH	Mannitol	13189207	1
Caesar & Loretz GmbH	Mannitol	14323119	1
Caesar & Loretz GmbH	Mannitol	17087915	1
Caesar & Loretz GmbH	Mannitol	18265502	1
Caesar & Loretz GmbH	Mannitol	17258819	1
Caesar & Loretz GmbH	Mannitol	17258820	1
Caesar & Loretz GmbH	Mannitol	18265408	2
Caesar & Loretz GmbH	Mannitol	18265420	5
Caesar & Loretz GmbH	Mannitol	18265417	3
Caesar & Loretz GmbH	Mannitol	18265409	1
Caesar & Loretz GmbH	Mannitol	18265431	1
Caesar & Loretz GmbH	Mannitol	18265505	1
Caesar & Loretz GmbH / ...	Mannitol	16200908	1
Caesar & Loretz GmbH/Kr...	Mannitol	18265432	3
Caesar/Ebert	Mannitol	17360108	1
ceal	Mannitol	17045006	1
cealo/phoenix	Mannitol	14323138	2
Celo	Mannitol	15197313	1
cesar&lorentz/Phönix	Mannitol	12305710	1
Defektur/eigen	Mannitol	1604008-01	1
Delta	Mannitol	1610027-01	1
Euro OTC	Mannitol	1708005	1
EuRho	Mannitol	1911M-01844	1
EuRho	Mannitol	1205016-01	1
EuRho	Mannitol	1211034-02	1
EuRho	Mannitol	1211034-01	1
EuRho	Mannitol	1404034-01	1
EuRho	Mannitol	1404034-02	2
EuRho	Mannitol	1502022-02	1
EuRho	Mannitol	1508012-01	6
EuRho	Mannitol	1511025-01	1
EuRho/GEHE	Mannitol	1409016-02	1
EuRho/GEHE	Mannitol	1409016-01	1
EuRho/Noweda	Mannitol	1703043-01	1
EuRho/Phoenix	Mannitol	1508012-01	1
EuRho/Sanac	Mannitol	1305043-01	1
Euro OTC	Mannitol	111100009-02	1
EuRhoPha	Mannitol	1404034-01	1
EURO	Mannitol	170401001	1
Euro OTC	Mannitol	16040008-01	1
Euro OTC	Mannitol	150801201	1
Euro OTC	Mannitol	160408-01	1
Euro OTC	Mannitol	1708005-02	3
Euro OTC	Mannitol	E671Z	1
Euro OTC	Mannitol	130504301	1
Euro OTC	Mannitol	1305043-02	14

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Supplier	Substance	Batch	Spectra
Euro OTC	Mannitol	1310004-01	14
Euro OTC	Mannitol	13189216	2
Euro OTC	Mannitol	140403402	2
Euro OTC	Mannitol	140403401	1
Euro OTC	Mannitol	1404036-02	1
Euro OTC	Mannitol	1409016-02	6
Euro OTC	Mannitol	150202201	2
Euro OTC	Mannitol	150202202	1
Euro OTC	Mannitol	158012-01	1
Euro OTC	Mannitol	1511025-01	38
Euro OTC	Mannitol	151102501	2
Euro OTC	Mannitol	151105-01	1
Euro OTC	Mannitol	1604008-01	34
Euro OTC	Mannitol	1604008	1
Euro OTC	Mannitol	150916M	1
Euro OTC	Mannitol	1604002-01	1
Euro OTC	Mannitol	160601-01	1
Euro OTC	Mannitol	161129M/1604008-01	1
Euro OTC	Mannitol	1610027-01	27
Euro OTC	Mannitol	160027-01	1
Euro OTC	Mannitol	170304301	2
Euro OTC	Mannitol	1704010-01	2
Euro OTC	Mannitol	170304302	1
Euro OTC	Mannitol	e118t	1
Euro OTC	Mannitol	1809008-02	4
Euro OTC	Mannitol	1901092	1
Euro OTC	Mannitol	1904025-01	2
Euro OTC	Mannitol	1806024/01	1
Euro OTC	Mannitol	1809008-01	5
Euro OTC	Mannitol	1708005-05	1
Euro OTC	Mannitol	1703043-01	13
Euro OTC	Mannitol	1110009-02	4
Euro OTC	Mannitol	1104028-01	1
Euro OTC	Mannitol	10112014E	1
Euro OTC	Mannitol	14003402	1
Euro OTC	Mannitol	15002022-01	1
Euro OTC	Mannitol	1502022-02	5
Euro OTC	Mannitol	150801	1
Euro OTC	Mannitol	1703049-01	1
Euro OTC	Mannitol	1610027-02	2
Euro OTC	Mannitol	1404034-01	15
Euro OTC	Mannitol	1110009-01	10
Euro OTC	Mannitol	1104028-03	3
Euro OTC	Mannitol	1205016-01	12
Euro OTC	Mannitol	1305043	1
Euro OTC	Mannitol	1409016-01	19
Euro OTC	Mannitol	T03-07/1409016-01	1
Euro OTC	Mannitol	1511024-01	1
Euro OTC	Mannitol	160400	2
Euro OTC	Mannitol	1211034-01	9
Euro OTC	Mannitol	1502022/01	1
Euro OTC	Mannitol	1205016-02	2
Euro OTC	Mannitol	E976E	2
Euro OTC	Mannitol	17087908	1
Euro OTC	Mannitol	1806024-1	1
Euro OTC	Mannitol	1708005-01	27
Euro OTC	Mannitol	17/14	1
Euro OTC	Mannitol	1310004-02	7
Euro OTC	Mannitol	12105433	3
Euro OTC	Mannitol	1508012-02	13

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Supplier	Substance	Batch	Spectra
Euro OTC	Mannitol	180200401	1
Euro OTC	Mannitol	180900802	1
Euro OTC	Mannitol	160603101	1
Euro OTC	Mannitol	1409016-1	1
Euro OTC	Mannitol	180219M/1708005-01	1
Euro OTC	Mannitol	1205016	1
Euro OTC	Mannitol	1902011-01	2
Euro OTC	Mannitol	19I20-F12	1
Euro OTC	Mannitol	1211034-02	14
Euro/Gehe	Mannitol	1508012-01	2
Euro/Noweda	Mannitol	1902011-01	2
Euro OTC	Mannitol	1305043-01	12
Euro OTC	Mannitol	16006031-01	1
Euro OTC	Mannitol	1606031-01	18
Euro OTC	Mannitol	1806024-01	5
Euro OTC	Mannitol	1006019-01	1
Euro OTC	Mannitol	13155710	1
Euro OTC	Mannitol	161002701	3
Euro OTC	Mannitol	1502022-01	15
Euro OTC	Mannitol	16H29-B02	1
Euro OTC	Mannitol	1703043-02	6
Euro OTC	Mannitol	E112N	1
Euro OTC	Mannitol	E118T	2
Euro OTC	Mannitol	1508012-01	27
Euro OTC	Mannitol	1610027-1	1
Euro OTC	Mannitol	1904025-02	1
Fagon	Mannitol	13K20-B01-292064	1
Fagron	Mannitol	11L19-N15	1
Fagron	Mannitol	1302C004	2
Fagron	Mannitol	1302C005	1
Fagron	Mannitol	13K20-B01-294194	2
Fagron	Mannitol	13E24N01	1
Fagron	Mannitol	13K20-B01	1
Fagron	Mannitol	13K20-B01-294193	1
Fagron	Mannitol	14G17-B06-301921	1
Fagron	Mannitol	12E24-N03	1
Fagron	Mannitol	14G04-B07	2
Fagron	Mannitol	14G04-B07-296196	1
Fagron	Mannitol	296196	1
Fagron	Mannitol	13K20-B01-287698	2
Fagron	Mannitol	14G04-B07-301693	1
Fagron	Mannitol	14G04-B07-301694	1
Fagron	Mannitol	15A26-B01-304717	4
Fagron	Mannitol	15I24-B04	1
Fagron	Mannitol	15K25-B04-317786	2
Fagron	Mannitol	16D20-B03-320486	1
Fagron	Mannitol	16D20-B03	1
Fagron	Mannitol	16G27-B03-324517	1
Fagron	Mannitol	16E11-B06	1
Fagron	Mannitol	16F27-B05-324516	1
Fagron	Mannitol	16D20-B04-320487	1
Fagron	Mannitol	17A27-B02	1
Fagron	Mannitol	17A27-B02-331292	4
Fagron	Mannitol	16H25-B03-326639	1
Fagron	Mannitol	16L15-B04-329317	2
Fagron	Mannitol	17D18-B03-335437	2
Fagron	Mannitol	17F27B04337912	1
Fagron	Mannitol	17F27-B07	2
Fagron	Mannitol	17/13-B04-340968	1
Fagron	Mannitol	17/13-B10	1

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Supplier	Substance	Batch	Spectra
Fagron	Mannitol	17F27-B04-337912	2
Fagron	Mannitol	17F27B04-337912	1
Fagron	Mannitol	17J23-B05-342007	2
Fagron	Mannitol	17123B05342007	1
Fagron	Mannitol	17J30-B09-343413	2
Fagron	Mannitol	720014-0001	1
Fagron	Mannitol	17F27-B07-338598	2
Fagron	Mannitol	17K29-B04-343940	1
Fagron	Mannitol	17K29-B05-345229	2
Fagron	Mannitol	17L04-B03-345230	1
Fagron	Mannitol	17J04-B06-341798	1
Fagron	Mannitol	17A12-B02	1
Fagron	Mannitol	18A30-B07-348872	2
Fagron	Mannitol	18D09-B13-352214	2
Fagron	Mannitol	18E25-B09-352755	2
Fagron	Mannitol	18E25-B07	1
Fagron	Mannitol	18G04-B13-354621	4
Fagron	Mannitol	18E25-B06-352505	1
Fagron	Mannitol	18J25-B08-356984	2
Fagron	Mannitol	17B08-B04-334313	1
Fagron	Mannitol	16F01-B03-322189	1
Fagron	Mannitol	17K29-B05	1
Fagron	Mannitol	18G04-B09	1
Fagron	Mannitol	19A14-B04-360505	1
Fagron	Mannitol	14G004-B07-301692	1
Fagron	Mannitol	18J04-B05-355467	4
Fagron	Mannitol	16/28-B01-328593	1
Fagron	Mannitol	12K28-N01	1
Fagron	Mannitol	14G04-B07-301685	1
Fagron	Mannitol	15B05-B04-304084	3
Fagron	Mannitol	17J30309-343413	1
Fagron	Mannitol	17D12-B01-334435	2
Fagron	Mannitol	16E11B07322830	1
Fagron	Mannitol	17I13-B04-340968	1
Fagron	Mannitol	18L03-B03	1
Fagron	Mannitol	19E06-B06-363488	1
Fagron	Mannitol	18A30-B08-346849	1
Fagron	Mannitol	15K17-B01-315560	2
Fagron	Mannitol	18E25-B08	1
Fagron	Mannitol	13K20-B01-287706	1
Fagron	Mannitol	19C11-B02-361201	1
Fagron	Mannitol	17I13-B03-340967	2
Fagron	Mannitol	19A14B04360505	1
Fagron	Mannitol	12J26-N15	1
Fagron	Mannitol	720014-0002	1
Fagron	Mannitol	18J25-B05-356984	1
Fagron	Mannitol	17B08-B02	2
Fagron	Mannitol	11219122	1
Fagron	Mannitol	16E11-B04	1
Fagron	Mannitol	17I13B03340967	1
Fagron	Mannitol	17I13-B10	1
Fagron	Mannitol	18D09-B11-351436	2
Fagron	Mannitol	17F27-B05-337913	1
Fagron	Mannitol	1502022-01	3
Fagron	Mannitol	14323121	1
Fagron	Mannitol	15K17-B03-314903	1
Fagron	Mannitol	16F27-B04-32483	1
Fagron	Mannitol	16H29-B02-326640	2
Fagron	Mannitol	16340301	1
Fagron	Mannitol	170612185	1

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Supplier	Substance	Batch	Spectra
Fagron	Mannitol	17A12-B02-332068	2
Fagron	Mannitol	17D18-B01	1
Fagron	Mannitol	17I13-B11-341331	1
Fagron	Mannitol	17/13-B11-341331	1
Fagron	Mannitol	17J30-B10-343414	1
Fagron	Mannitol	E911K	1
Fagron	Mannitol	14G04-B07-301692	10
Fagron	Mannitol	19C11-B05-361204	1
Fagron	Mannitol	16212103	1
Fagron	Mannitol	16G27-B05-325659	1
Fagron	Mannitol	17C28-B06	2
Fagron	Mannitol	18B23-B10-349553	2
Fagron	Mannitol	18J25-B07-356983	1
Fagron	Mannitol	18L03-B06-357782	1
Fagron	Mannitol	18L21-B04-358870	1
Fagron	Mannitol	18L21-B05-358871	2
Fagron	Mannitol	19A14-B03-360504	1
Fagron	Mannitol	17045002	1
Fagron	Mannitol	15K25-B06-318740	3
Fagron	Mannitol	16B24-B09-320013	2
Fagron	Mannitol	16E11-B07-322830	2
Fagron	Mannitol	16H29-B05-327813	1
Fagron	Mannitol	16L15-B04	1
Fagron	Mannitol	E833Z	1
Fagron	Mannitol	17C28-B03-333349	1
Fagron	Mannitol	17J30-B11-343939	1
Fagron	Mannitol	17C28-B05-33361	1
Fagron	Mannitol	12E24-N08	1
Fagron/ Noweda	Mannitol	15A26-B01-304717	1
Fragon	Mannitol	18D09-B13-352214	1
FragonFiebig	Mannitol	18A30-B07-348872	2
Fragron/ Alliance	Mannitol	19C11-B04	1
Fragron/Noweda	Mannitol	17A12-B04-330729	1
Gatt-Koller	Mannitol	1803827	2
Gehe	Mannitol	12E24-N08	1
Gehe	Mannitol	12J26-N15	1
Gehe	Mannitol	13E24-N01	1
Gehe	Mannitol	1508012-01	1
Gehe	Mannitol	15197313	1
Gehe	Mannitol	16200913	1
Gehe	Mannitol	17F27-B05-337913	1
Gehe	Mannitol	17L04-B03-345230	1
Gehe	Mannitol	17258812	1
Gehe	Mannitol	19B12-B02-359604	1
GEHE	Mannitol	130504301	1
GEHE	Mannitol	17B08-B04-334312	1
GEHE	Mannitol	17258808	1
gehe 10.12.13	Mannitol	1305043/01	1
GEHE 24.07.2014	Mannitol	1310004-02	1
Gehe/ Eurho	Mannitol	1205016-02	1
Caelo	Mannitol	12105433	6
Caelo	Mannitol	1310004-01	3
Caelo	Mannitol	16200916	2
Gehe/Euro	Mannitol	1511025-01	1
Euro OTC	Mannitol	1802004-01	17
Fagron	Mannitol	13B01-B05-283812	1
Fagron	Mannitol	16H02-B01-325660	1
Fagron	Mannitol	16H29-B03-326641	1
Fagron	Mannitol	17A12-B03	1
Gutenberg-Apotheke	Mannitol	1310004-01	4

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Supplier	Substance	Batch	Spectra
Gutenberg-Apotheke	Mannitol	13189221	1
Gutenberg-Apotheke	Mannitol	1310004-02	1
Hirsch	Mannitol	12305725	1
JENNE	Mannitol	17258811	1
Klenk	Mannitol	1211034-02	2
Klenk	Mannitol	5224A110314	1
Klenk	Mannitol	1606031-01	2
Kögl	Mannitol	1900820	1
Linden-Apotheke	Mannitol	1205016-02	1
Noewda	Mannitol	15197319	1
Noweda	Mannitol	11219101	2
Noweda	Mannitol	11219138	1
Noweda	Mannitol	12105404	1
Noweda	Mannitol	1305043-01	1
Noweda	Mannitol	14323124	1
Noweda	Mannitol	15124-B05-314323	1
Noweda	Mannitol	15124-B05-314323	1
Noweda	Mannitol	15K17-B01	1
Noweda	Mannitol	15B05-B06-304302	1
Noweda	Mannitol	16D20-B04-320487	1
Noweda	Mannitol	1508012-01	1
Noweda	Mannitol	16L15-B05-329316	1
Noweda	Mannitol	P101P102P103	3
Noweda	Mannitol	1708005-01	3
Noweda	Mannitol	1904025-01	1
Noweda	Mannitol	1809008-02	1
Noweda	Mannitol	19D16-B03	1
Noweda	Mannitol	1205016-02	2
Caelo	Mannitol	12305736	4
Caelo	Mannitol	16H29-B05-327813	1
Noweda29.04.2015	Mannitol	14323113	1
Euro OTC	Mannitol	1404034-02	15
Euro OTC	Mannitol	1606031-02	8
Phagron	Mannitol	1302C004-279405	1
Phoenix	Mannitol	120501602	1
Phoenix	Mannitol	1310004-01	1
Phoenix	Mannitol	15197314	1
Phoenix	Mannitol	1708005-01	2
Phoenix	Mannitol	18265503	1
Phoenix	Mannitol	18265506	1
Phoenix	Mannitol	19C11-B03-361202	1
Phoenix	Mannitol	18L21-B04-358870	1
Phoenix	Mannitol	19B12-B03	1
PHOENIX 24.04.2014	Mannitol	1310004-01	3
Fagron	Mannitol	19I20-F09-366392	1
Phoenix WE 10.03.17 EK...	Mannitol	16340302	1
Caelo	Mannitol	16L15-B04-329317	1
Caelo	Mannitol	16200909	1
phönix	Mannitol	14323138	1
phönix	Mannitol	15197313	2
Phönix	Mannitol	120501602	1
Phönix	Mannitol	12305723	1
Phönix	Mannitol	1211034-02	1
Phönix	Mannitol	1305043-01	1
Phönix	Mannitol	14051215	1
Phönix	Mannitol	16200924	2
Phönix	Mannitol	17360109	1
Phönix	Mannitol	18L21-B04	1
PHÖNIX	Mannitol	16212102	1
PHÖNIX	Mannitol	17258823	2

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Supplier	Substance	Batch	Spectra
PHÖNIX	Mannitol	17258821	1
PHÖNIX	Mannitol	16200923	1
Phönix WE:02.08.2016 ...	Mannitol	15197313	1
Caelo	Mannitol	17258809	5
Caelo	Mannitol	15197313	15
Primavera/Phoenix	Mannitol	1708005-01	1
Roquette Lestrem/Noweda	Mannitol	1508012-01	1
Roquette Lestrem/Noweda	Mannitol	1511025-01	1
Sana	Mannitol	17258809	2
Sanac	Mannitol	1610027-01	1
Sanacorp	Mannitol	1310004-01	1
Sanacorp	Mannitol	13189215	1
Sanacorp	Mannitol	16200903	1
Sanacorp	Mannitol	16200924	1
Sanacorp	Mannitol	17087916	1
Sanacorp	Mannitol	17258809	1
Sanacorp	Mannitol	17258808	1
Sanacorp E.K:19,49 -25...	Mannitol	17045009	1
Caelo	Mannitol	1205016-01	2
Caelo	Mannitol	18265508	5
Caelo	Mannitol	15197301	13
Caelo	Mannitol	14323113	1
stumpf	Mannitol	1104028-02	1
VDL;21.11.14;3,98EUR	Mannitol	13189227	1
WE:16.03.2016 Sanacorp	Mannitol	14323124	1
WE:30.03.2016 Sanacorp	Mannitol	14323138	1
WE:Sanacorp 02.09.16 ...	Mannitol	16212101	1
WE:Sanacorp 25.10.2016 ...	Mannitol	16212102	2
xxxxx	Mannitol	xxxx	1
Caelo	Mannitol	12305723	4
Sonnen-Apotheke Wefensl...	Mannitol		1

- 109 689 spectra from 742 *Apo-Ident* customers from a total of 31 463 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mannitol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mannitol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	1009	1	118 052
Type C	0	1554	4	109 674

The substance/substance group *Mannitol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	99.9010 % (> 99.6040 %)
Type C	100.0000 % (> 99.8897 %)	99.7433 % (> 99.5507 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mannitol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	41.59	—
Potassium citrate	54.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mannitol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20980	20980	0.00	38.22
21884	21884	0.00	38.62
22286	22286	0.00	39.68
22581	22286	2.13	39.75
22883	22286	2.18	39.24
22884	21884	2.52	38.90
24579	21884	5.10	40.01

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Melatonin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20553-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Melatonin; Melatoninum

Special notes

When selecting the *Melatonin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Melatonin	9	7	197

Second-stage model

For differentiation of the substance/substance group *Melatonin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Melatonin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Melatonin	12321404	20834	40	20121107
Caelo	Melatonin	12321411	20835	40	20121107
Caelo	Melatonin	12321415	20987	80	20121107
Euro OTC	Melatonin	1305029-02	21618	60	1411054
Euro OTC	Melatonin	1510041	22237	60	20151123*
Euro OTC	Melatonin	1709020	23889	40	20180105*
Euro OTC	Melatonin	1804015	24128	40	20180522*
Euro OTC	Melatonin	1804015	24128SI	40	20180522*
Fagron	Melatonin	15G06-B03-315183	22892	40	20150717
Fagron	Melatonin	15G06-B03-323733	22893	40	20150717

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 480 spectra of 10 reference samples from the substance/substance group *Melatonin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 209 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 539 spectra of 13 reference samples from the substance/substance group *Melatonin*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Melatonin	163437	23036	40
Caelo	Melatonin	190946	24519	40
Euro OTC	Melatonin	1610040	22871	40
Euro OTC	Melatonin	1811004	24330	40
Euro OTC	Melatonin	1906031	24767	40
Euro OTC	Melatonin	1906030	24802	40
Euro OTC	Melatonin	1909031	24924	40
Caelo	Melatonin	163437	23036SI	40
Caelo	Melatonin	190946	24519SI	40
Euro OTC	Melatonin	1510041	22237SI [†]	60
Euro OTC	Melatonin	1811004	24330SI	39
Fagron	Melatonin	15G06-B03-315183	22892SI [†]	40
Fagron	Melatonin	15G06-B03-323733	22893SI [†]	40

- 118 603 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 610 spectra from 194 *Apo-Ident* customers from 204 batches from the substance/substance group *Melatonin*.
- Among them are spectra of independent samples from 197 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance	Melatonin	15254307	3
Alliance	Melatonin	15254316	1
allianz	Melatonin	15254324	1
Alte Apotheke	Melatonin	15254328	1
Anzag	Melatonin	12321415	1
apo ident	Melatonin	1610040-02	1
Audor Pharma	Melatonin	ALC/MLT/170901	1
Bombastus	Melatonin	18210304	1
Caelo	Melatonin	16343705	1
Caelo	Melatonin	11267122	1
Caelo	Melatonin	1126109	1
Caelo	Melatonin	11267109	1
Caelo	Melatonin	11267119	1
Caelo	Melatonin	20021312	1
Caelo	Melatonin	2313M03554	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Melatonin	11267126	2
Caelo	Melatonin	10071303	1
Caelo	Melatonin	12321416	5
Caelo	Melatonin	16121303	1
Caelo	Melatonin	13167309	1
Caelo	Melatonin	14110302	2
Caelo	Melatonin	15093004	2
Caelo	Melatonin	13167312	3
Caelo	Melatonin	20021505	1
Caelo	Melatonin	13167314	5
Caelo	Melatonin	15093002	2
Caelo	Melatonin	15093008	8
Caelo	Melatonin	15254305	7
Caelo	Melatonin	15254307	12
Caelo	Melatonin	15254319	10
Caelo	Melatonin	160125M	1
Caelo	Melatonin	15254336	4
Caelo	Melatonin	15254327	1
Caelo	Melatonin	15254333	1
Caelo	Melatonin	15254332	2
Caelo	Melatonin	16266908	4
Caelo	Melatonin	16266904	3
Caelo	Melatonin	15254325	1
Caelo	Melatonin	16266909	9
Caelo	Melatonin	16343710	11
Caelo	Melatonin	16343709	6
Caelo	Melatonin	16343708	9
Caelo	Melatonin	17305102	17
Caelo	Melatonin	1709020-01	1
Caelo	Melatonin	17305110	5
Caelo	Melatonin	17305105	9
Caelo	Melatonin	163437/13	1
Caelo	Melatonin	26051805	1
Caelo	Melatonin	17305113	6
Caelo	Melatonin	17305118	5
Caelo	Melatonin	17305114	3
Caelo	Melatonin	17/28-B04-345376	2
Caelo	Melatonin	17305119	3
Caelo	Melatonin	18210304	8
Caelo	Melatonin	17350119	1
Caelo	Melatonin	182010312	1
Caelo	Melatonin	18210318	2
Caelo	Melatonin	14110305	2
Caelo	Melatonin	14110308	3
Caelo	Melatonin	15254320	3
Caelo	Melatonin	15254338	6
Caelo	Melatonin	17305101-20180206Ma1	1
Caelo	Melatonin	16343713	10
Caelo	Melatonin	18210312	1
Caelo	Melatonin	18210319	2
Caelo	Melatonin	17305116	2
Caelo	Melatonin	14110316	1
Caelo	Melatonin	17305122	7
Caelo	Melatonin	1514E-03554	1
Caelo	Melatonin	12321422	4
Caelo	Melatonin	19128006	8
Caelo	Melatonin	12321406	1
Caelo	Melatonin	13167301	8
Caelo	Melatonin	15093010	5
Caelo	Melatonin	150601	1

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Supplier	Substance	Batch	Spectra
Caelo	Melatonin	17305106	3
Caelo	Melatonin	15G06-B03-323733	1
Caelo	Melatonin	18210306	6
Caelo	Melatonin	11267121	1
Caelo	Melatonin	14110314	2
Caelo	Melatonin	15254324	4
Caelo	Melatonin	16343707	2
Caelo	Melatonin	120009	1
Caelo	Melatonin	11267110	1
Caelo	Melatonin	11267120	4
Caelo	Melatonin	12321421	2
Caelo	Melatonin	13167302	1
Caelo	Melatonin	15093001	7
Caelo	Melatonin	15093013	2
Caelo	Melatonin	1524309	1
Caelo	Melatonin	15G06-B03-321299	1
Caelo	Melatonin	16343706	1
Caelo	Melatonin	13167310	1
Caelo	Melatonin	11267111	1
Caelo	Melatonin	11267102	1
Caelo	Melatonin	15254306	8
Caelo	Melatonin	15254308	7
Caelo	Melatonin	15254321	6
Caelo	Melatonin	15254331	4
Caelo	Melatonin	15254328	2
Caelo	Melatonin	117305118	1
Caelo	Melatonin	18210313	2
Caelo	Melatonin	18210311	4
Caelo	Melatonin	19128005	3
Caelo	Melatonin	17305121	1
Caelo	Melatonin	15C20B01306077	1
Caelo	Melatonin	16343711	3
Caelo	Melatonin	17305104	1
Caelo	Melatonin	191280002	1
Caelo	Melatonin	15093012	2
Caelo	Melatonin	17305101	3
Caelo	Melatonin	16343702	1
Caelo	Melatonin	17305115	1
Caelo	Melatonin	17305120	1
Caelo	Melatonin	18210308	1
Caelo	Melatonin	18210315	1
Caelo	Melatonin	19128003	2
Caelo	Melatonin	15254313	2
Caelo	Melatonin	16266906	1
Caelo	Melatonin	18210301	7
Caelo	Melatonin	18210307	3
Caelo	Melatonin	19128007	3
Caesar & Lorenz GmbH	Melatonin	17305106	1
Caesar & Loretz GmbH	Melatonin	17305105	1
Caesar & Loretz GmbH	Melatonin	1524517305113	1
Caesar & Loretz GmbH	Melatonin	17305106	1
Caesar & Loretz GmbH	Melatonin	18210305	1
Caesar & Loretz GmbH	Melatonin	191280001	1
Caesar & Loretz GmbH / ...	Melatonin	17305102	2
Caesar & Loretz GmbH / ...	Melatonin	17305106	1
Caesar & Loretz GmbH / ...	Melatonin	18210306	1
Cealo	Melatonin	12321422	1
Cealo/Gehe	Melatonin	10296624	1
Euro OTC	Melatonin	1407028-02	3
Euro OTC	Melatonin	151004101	3

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Supplier	Substance	Batch	Spectra
Euro OTC	Melatonin	161004001	1
Euro OTC	Melatonin	180401501	1
Euro OTC	Melatonin	1204003-02	12
Euro OTC	Melatonin	12001	2
Euro OTC	Melatonin	120400302	1
Euro OTC	Melatonin	1610040-01	2
Euro OTC	Melatonin	1709020-01	11
Euro OTC	Melatonin	17305106	1
Euro OTC	Melatonin	120008	1
Euro OTC	Melatonin	1305029-01	8
Euro OTC	Melatonin	1906030-01	3
Euro OTC	Melatonin	15254316	1
Euro OTC	Melatonin	1804015-01	3
Euro OTC	Melatonin	1407028-01	1
Euro OTC	Melatonin	1510041-01	5
Euro OTC	Melatonin	1610040-02	5
Fagron	Melatonin	11F09-N02	1
Fagron	Melatonin	12K13-N02	1
Fagron	Melatonin	13D12-N10	2
Fagron	Melatonin	13D12N10	1
Fagron	Melatonin	13e22-n12	1
Fagron	Melatonin	13E22N12	1
Fagron	Melatonin	13H21-N06	3
Fagron	Melatonin	14G18-B01-297245	1
Fagron	Melatonin	13H29-B03-291180	2
Fagron	Melatonin	14G18-B01-297242	1
Fagron	Melatonin	13E22-N12	1
Fagron	Melatonin	14G18-B01-297244	1
Fagron	Melatonin	15C20-B01-306078	3
Fagron	Melatonin	15G06-B03-321298	3
Fagron	Melatonin	16G06-B01-327131	3
Fagron	Melatonin	16G06-B01-324743	2
Fagron	Melatonin	16343702	1
Fagron	Melatonin	17/28-B04-344440	2
Fagron	Melatonin	17C22-B01-337089	2
Fagron	Melatonin	17128-B04-344439	1
Fagron	Melatonin	17128-B04	1
Fagron	Melatonin	17I28-B04-348747	1
Fagron	Melatonin	17/28-B04-344438	2
Fagron	Melatonin	15C20-B01-306077	1
Fagron	Melatonin	15C20-B01-327131	1
Fagron	Melatonin	16G06-B01-329142	2
Fagron	Melatonin	120009	2
Fagron	Melatonin	15G06-B03-321299	3
Fagron	Melatonin	17I28-B04-344440	1
Fagron	Melatonin	13H21-N065x	1
Fagron	Melatonin	17I28-B04	1
Fagron	Melatonin	1305029-01	1
Fagron	Melatonin	13H29-B03	1
Fagron	Melatonin	15C20-B01-308426	3
Fagron	Melatonin	17C22-B01-337091	1
Fagron	Melatonin	12G19-N03	1
Fagron	Melatonin	15C20-B01-308427	5
Fagron	Melatonin	15G06-B03-318398	1
Fagron	Melatonin	17C22-B01-337090	3
Fagron	Melatonin	17I28-B04-347314	1
Fagron	Melatonin	17I28-B04-351312	2
Fagron	Melatonin	17I28-B04-356971	2
Fagron	Melatonin	16343708	1
Fargon GmbH & Co.KG	Melatonin	16G06-B01-324743	1

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Supplier	Substance	Batch	Spectra
Farmalabor	Melatonin	P1800033-000	1
Farmalabor	Melatonin	R1804925	1
Farmalabor / Farmalabor	Melatonin	P1201556-000	1
Fgron	Melatonin	12G19-N03	1
Gehe	Melatonin	11L21-N04	1
Gehe	Melatonin	11/26-N07	1
Gehe	Melatonin	12G19-N03	2
Gehe	Melatonin	13D12-N10	1
Gehe	Melatonin	13E22-N12	1
Gehe	Melatonin	15254324	1
Gehe	Melatonin	1510041-01	1
Gehe	Melatonin	18210320	1
Gehe	Melatonin	19128003	5
Gehe	Melatonin	18210311	1
GEHE	Melatonin	17I28-B04	1
GEHE	Melatonin	17I-28-B04	1
GEHE 22.03.2014	Melatonin	13167302	1
Caelo	Melatonin	16266903	2
gepepharm	Melatonin	15G06-B03-315183	1
Inresa	Melatonin	110005	1
Caelo	Melatonin	17I28-B04-345376	1
Koisser	Melatonin	140202	2
KS Pharma	Melatonin	XPS130428	1
Fagron	Melatonin	17I28-B04-344439	2
Phoenix	Melatonin	15C20-B01	1
Phoenix	Melatonin	16266903	1
Phoenix	Melatonin	18210315	1
Phoenix	Melatonin	3368	1
Phoenix 03.04.2014	Melatonin	12J19-N02	1
PHOENIX 14.04.2014	Melatonin	13E22-N12	1
phönix	Melatonin	15254308	1
Phönix	Melatonin	11267111	1
Phönix	Melatonin	APALC/MCT17030111	1
Phönix	Melatonin	17305115	1
Phönix	Melatonin	18210303	2
Phönix 02.01.15	Melatonin	13H21-N06	1
Phönix 02.01.2014	Melatonin	1204003-02	1
Phönix 19.02.2014	Melatonin	13167301	2
Caelo	Melatonin	15G06-B03-321298	2
Caelo	Melatonin	16266901	7
sanacorp	Melatonin	14110320	1
Sanacorp	Melatonin	11267119	1
Sanacorp	Melatonin	161004001	1
Sanacorp	Melatonin	161004002	1
Sanacorp	Melatonin	APALC/MLT/161101M	1
Sanacorp	Melatonin	APALC/MLT/170301M	2
Sanacorp	Melatonin	MLT/SEP/170901	1
Sanacorp	Melatonin	APMLT170901M	1
Sanacorp	Melatonin	APALC/MLT/170901M	1
Sanacorp	Melatonin	18210318	1
Sanacorp WE: 17.0518 EK...	Melatonin	1709020-01	1
Sanaorp	Melatonin	16343707	1
WE Sanacorp 28.11..2016...	Melatonin	15254324	1
Fagron	Melatonin	15G06-B03-315183	5
Caelo	Melatonin	12321404	3
Caelo	Melatonin	12321415	3
Caelo	Melatonin	12321411	1
Fagron	Melatonin	15G06-B03-323733	1
Sanacorp	Melatonin		1

- 110 637 spectra from 742 *Apo-Ident* customers from a total of 31 687 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Melatonin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Melatonin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	480	0	110 209
Type B	0	539	0	118 603
Type C	0	580	30	110 637

The substance/substance group *Melatonin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8868 %)
Type C	100.0000 % (> 99.8899 %)	95.0820 % (> 94.5902 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Melatonin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	34.49	—
Levothyroxin sodium	45.94	—
Choline hydrogen tartrate	48.98	—
Ambroxol hydrochloride	49.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Melatonin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20987	21618	3.72	48.43
21618	21618	0.00	48.44
22892	22237	1.89	47.49
22893	22237	2.67	47.28
24128	24128	0.00	46.96
20834	24128	16.45	55.18
20835	22237	4.13	48.43
22237	22237	0.00	47.62
23889	23889	0.00	47.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Menthol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20036-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Menthol; Mentholum

Special notes

When selecting the *Menthol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Menthol	8	10	254

Second-stage model

For differentiation of the substance/substance group *Menthol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Menthol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Menthol	13377404	21443	60	20131212
Caelo	Menthol	181522	24233	40	20180625*
Euro OTC	Menthol	1403022-02	21601	45	20140408
Euro OTC	Menthol	1509045	21932	60	20151008*
Euro OTC	Menthol	1603024	22657	40	20160429*
Euro OTC	Menthol	1608012	22825	40	20160902*
Fagron	Menthol	16L20-T04-044769	23596	40	20170116
Fagron	Menthol	18L04-T06-065445	24690	40	20181217

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 365 spectra of 8 reference samples from the substance/substance group *Menthol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 324 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 475 spectra of 12 reference samples from the substance/substance group *Menthol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Menthol	160956	22452	60
Caelo	Menthol	170927	23312	40
Caelo	Menthol	171889	23668	40
Caelo	Menthol	183286	24666	40
Caelo	Menthol	192453	24877	40
Euro OTC	Menthol	1701014	23005	40
Euro OTC	Menthol	1705022	23427	40
Euro OTC	Menthol	1802003	23951	40
Euro OTC	Menthol	1905013	24599	40
Euro OTC	Menthol	1912006	25089	40
Caelo	Menthol	170927	23645	40
Euro OTC	Menthol	1403022-02	21601 [†]	15

- 118667 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1067 spectra from 493 *Apo-Ident* customers from 261 batches from the substance/substance group *Menthol*.
- Among them are spectra of independent samples from 254 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Menthol	1305010-01	1
AHD	Menthol	18128014	1
Caelo	Menthol	1087209	1
Euro OTC	Menthol	15020006-02	1
Euro OTC	Menthol	1701014-01	13
Alliance Health 14.04..14	Menthol	1305010-02	1
Andreas Imhof	Menthol	8052015	1
Anzag	Menthol	12/19-N10	1
Anzag	Menthol	16L20-T04-044769	1
Euro OTC	Menthol	1608012-12	1
Fagron	Menthol	1219-N10	1
Apo-ident	Menthol	1509045-03	1
beyvers	Menthol	16095613	1
Caelo	Menthol	11202910	5
Caelo	Menthol	12020402	5
Caelo	Menthol	7111201	1
Caelo	Menthol	1202041	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Menthol	10008029-02	1
Caelo	Menthol	20200712-2	1
Caelo	Menthol	1204036-01	1
Caelo	Menthol	12020411	8
Caelo	Menthol	12246205	8
Caelo	Menthol	12246204	1
Caelo	Menthol	12020410	1
Caelo	Menthol	25051301	1
Caelo	Menthol	13103901	24
Caelo	Menthol	130501001	1
Caelo	Menthol	IntCh311052	1
Caelo	Menthol	750137	1
Caelo	Menthol	12246211	3
Caelo	Menthol	13159105	19
Caelo	Menthol	72173258	1
Caelo	Menthol	13G09-N09	1
Caelo	Menthol	29121103	1
Caelo	Menthol	687711	1
Caelo	Menthol	25041402	1
Caelo	Menthol	19051401	1
Caelo	Menthol	11091405	1
Caelo	Menthol	13377409	9
Caelo	Menthol	13377407	2
Caelo	Menthol	1410004-01	2
Caelo	Menthol	1403022-01	1
Caelo	Menthol	13377412	3
Caelo	Menthol	13377413	1
Caelo	Menthol	1403022-02	1
Caelo	Menthol	13103802	1
Caelo	Menthol	14183017	3
Caelo	Menthol	15076101	7
Caelo	Menthol	14183014	2
Caelo	Menthol	15076115	2
Caelo	Menthol	1507601	1
Caelo	Menthol	15363803	2
Caelo	Menthol	930716	1
Caelo	Menthol	15363809	7
Caelo	Menthol	160719M	1
Caelo	Menthol	15363810	13
Caelo	Menthol	16095602	2
Caelo	Menthol	161202M/15076111	1
Caelo	Menthol	16095606	14
Caelo	Menthol	16095604	1
Caelo	Menthol	15286216	1
Caelo	Menthol	16095609	1
Caelo	Menthol	2416	1
Caelo	Menthol	1705022-01	5
Caelo	Menthol	1701014-02	2
Caelo	Menthol	160956	1
Caelo	Menthol	62470307	1
Caelo	Menthol	171889035483	1
Caelo	Menthol	17188906	2
Caelo	Menthol	16095617	1
Caelo	Menthol	17328803	3
Caelo	Menthol	16081805	1
Caelo	Menthol	1046973	2
Caelo	Menthol	19091805	1
Caelo	Menthol	18128007	1
Caelo	Menthol	17351506	1
Caelo	Menthol	18128015	8

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Supplier	Substance	Batch	Spectra
Caelo	Menthol	18328605	4
Caelo	Menthol	18152214	1
Caelo	Menthol	19162801	2
Caelo	Menthol	17078004	1
Caelo	Menthol	11202901	1
Caelo	Menthol	15286205	1
Caelo	Menthol	15363815	13
Caelo	Menthol	170822M/16095616	1
Caelo	Menthol	12246203	1
Caelo	Menthol	13159110	2
Caelo	Menthol	14183006	1
Caelo	Menthol	16098614	1
Caelo	Menthol	16095613	13
Caelo	Menthol	14183004	13
Caelo	Menthol	14183008	3
Caelo	Menthol	90(17328804)	1
Caelo	Menthol	91(18128009)	1
Caelo	Menthol	92(18128015)	1
Caelo	Menthol	15363804	11
Caelo	Menthol	1701014-01	2
Caelo	Menthol	1802003-01	3
Caelo	Menthol	14183012	3
Caelo	Menthol	170502201	1
Caelo	Menthol	16L20-T04-053177	1
Caelo	Menthol	13D1N09	1
Caelo	Menthol	18328601	1
Caelo	Menthol	16095614	12
Caelo	Menthol	5117A-01855	1
Caelo	Menthol	15363805	9
Caelo	Menthol	17188903	17
Caelo	Menthol	15076113	7
Caelo	Menthol	17328804	14
Caelo	Menthol	13377402	3
Caelo	Menthol	15286212	1
Caelo	Menthol	15076112	10
Caelo	Menthol	15076219	1
Caelo	Menthol	10157615	1
Caelo	Menthol	13159104	4
Caelo	Menthol	15286209	1
Caelo	Menthol	17078006	1
Caelo	Menthol	192977004	1
Caelo	Menthol	133774112	1
Caelo	Menthol	16095620	8
Caelo	Menthol	1738804	1
Caelo	Menthol	14183011	1
Caelo	Menthol	15076104	1
Caelo	Menthol	16095616	1
Caelo	Menthol	170101402	1
Caelo	Menthol	15076118	1
Caelo	Menthol	17078009	1
Fagron	Menthol	16L20-T04-053177	7
Fagron	Menthol	1807044-01	1
Caelo	Menthol	1608012-02	3
Caelo	Menthol	3912A-01855	1
Caelo	Menthol	1536815	1
Caelo	Menthol	1320260	2
Caelo	Menthol	314Q01855	1
Caelo	Menthol	814A-01855	1
Caelo	Menthol	515M-01855	1
Caelo	Menthol	15076215	1

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Supplier	Substance	Batch	Spectra
Caelo	Menthol	1509045-03	1
Caelo	Menthol	5315I-01855	1
Caelo	Menthol	16095603	3
Caelo	Menthol	160956217188904	1
Caelo	Menthol	17351505	4
Caelo	Menthol	18128009	10
Caelo	Menthol	18152205	1
Caelo	Menthol	18152216	1
Caelo	Menthol	1410004-02	1
Caelo	Menthol	13377408	2
Caelo	Menthol	14183020	1
Caelo	Menthol	1603024-01	3
Caelo	Menthol	17351501	1
Caelo	Menthol	16095619	14
Caecolo/Gehe	Menthol	16096619	1
Caesar & Loretz	Menthol	15363809	1
Caesar & Loretz GmbH	Menthol	17328804	1
Caesar & Loretz GmbH	Menthol	18128007	1
Caesar & Loretz GmbH	Menthol	19162801	1
Caesar & Loretz GmbH	Menthol	18328604	1
Caesar & Loretz GmbH, 4...	Menthol	11202910	1
Caesar & Loretz GmbH, 4...	Menthol	12020402	1
Caesar & Loretz GmbH, 4...	Menthol	12020411	1
Caesar & Loretz GmbH, 4...	Menthol	13103901	1
Caesar & Loretz GmbH/No...	Menthol	18152202	1
Caesar&Loretz,Phönix	Menthol	15076106	1
Caesar/Noweda	Menthol	12020403	1
Caesar/Noweda	Menthol	12246211	1
Caesar/Noweda	Menthol	15076111	2
Cealo	Menthol	1705022-01	1
E Plus	Menthol	1705022-01	1
Eurho	Menthol	170502201	1
EuRho	Menthol	2910A-01855	1
EuRho	Menthol	1204036-02	1
EuRho	Menthol	1305010-01	1
EuRho	Menthol	915A-01855	1
EuRho	Menthol	1603024-01	1
EuRho	Menthol	1701014-02	1
EuRho	Menthol	1705022-01	2
EuRho	Menthol	1046973	1
Euro OTC	Menthol	1705022-01	24
EuRho/Alliance	Menthol	1701014-01	1
Euro OTC	Menthol	1509045-03	9
Euro OTC	Menthol	1802003/01	1
Euro OTC	Menthol	170101401	1
Euro OTC	Menthol	1305010-02	6
Euro OTC	Menthol	130501002	1
Euro OTC	Menthol	1002019-03	1
Euro OTC	Menthol	14030222-02	1
Euro OTC	Menthol	1502006-01	16
Euro OTC	Menthol	150200601	1
Euro OTC	Menthol	1502006-02	16
Euro OTC	Menthol	1509045-02	11
Euro OTC	Menthol	1603021-01	1
Euro OTC	Menthol	1602024-01	1
Euro OTC	Menthol	160801201	2
Euro OTC	Menthol	20116	1
Euro OTC	Menthol	1608012-1	1
Euro OTC	Menthol	18121718	1
Euro OTC	Menthol	170502201	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Menthol	1146105	2
Euro OTC	Menthol	1807044_01	1
Euro OTC	Menthol	1701014_01	1
Euro OTC	Menthol	1204036-02	3
Euro OTC	Menthol	696773	1
Euro OTC	Menthol	1210017-02	11
Euro OTC	Menthol	1204036-1	1
Euro OTC	Menthol	6102014B	1
Euro OTC	Menthol	25021709	1
Euro OTC	Menthol	1608012-02	13
Euro OTC	Menthol	170101402	3
Euro OTC	Menthol	16L20-T04-053177	1
Euro OTC	Menthol	1905013-01	5
Euro OTC	Menthol	1204036-01	8
Euro OTC	Menthol	120403602	1
Euro OTC	Menthol	1305010-01	7
Euro OTC	Menthol	807862	1
Euro OTC	Menthol	1603024-01	35
Euro OTC	Menthol	1046973	1
Euro OTC	Menthol	973192	2
Euro OTC	Menthol	1111020-01	1
Euro OTC	Menthol	1807044-01	15
Euro OTC	Menthol	PM14	1
Euro OTC	Menthol	1905013-02	2
Euro OTC	Menthol	1403022-01	2
Euro OTC	Menthol	1502006	1
Euro OTC	Menthol	180704401	1
Euro OTC	Menthol	120-4036-02	2
Euro OTC	Menthol	1008029-01	1
Euro OTC	Menthol	1105028-01	1
Euro OTC	Menthol	1509045-01	4
Euro OTC	Menthol	1608012-01	22
Euro OTC	Menthol	141000401	1
Euro OTC	Menthol	1310J-01855	1
Euro OTC	Menthol	1410004-01	15
Euro OTC	Menthol	140322-01	1
Euro OTC	Menthol	1701014-2	1
Euro OTC	Menthol	1705022011	1
Euro OTC	Menthol	1807044-02	2
Euro Ph. / Gehe	Menthol	1701014-02	1
Euro OTC	Menthol	1701014-02	19
Euro OTC	Menthol	1210017-01	4
Euro OTC	Menthol	140302201	2
Euro OTC	Menthol	1410004-02	10
Euro OTC	Menthol	180200301	2
Euro OTC	Menthol	150904502	1
Euro OTC	Menthol	1001505	2
Euro OTC	Menthol	1802003-01	25
Euro OTC	Menthol	17050022-01	1
Euro OTC	Menthol	1987209	1
Europharm	Menthol	130501-01	1
Fagron	Menthol	11C01-N01	1
Fagron	Menthol	12Cos-N03	1
Fagron	Menthol	12D23-N06	6
Fagron	Menthol	12F01-N14	2
Fagron	Menthol	12G20-N02	3
Fagron	Menthol	11G19-N07	1
Fagron	Menthol	13D16-N09	7
Fagron	Menthol	13G09-N090204/520	1
Fagron	Menthol	13G09-N09	1

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Supplier	Substance	Batch	Spectra
Fagron	Menthol	13J21-N04	2
Fagron	Menthol	14H29-M02	10
Fagron	Menthol	778301	1
Fagron	Menthol	14100041-01	1
Fagron	Menthol	15076115	1
Fagron	Menthol	1701014-02	1
Fagron	Menthol	16L20-To4	1
Fagron	Menthol	18G02-T30	2
Fagron	Menthol	18L04-T06	1
Fagron	Menthol	16120T04-053177	1
Fagron	Menthol	12/19-N100554/560	1
Fagron	Menthol	12/19-N10	1
Fagron	Menthol	14H29-M04	1
Fagron	Menthol	750137	1
Fagron	Menthol	16L20T04044769	1
Fagron	Menthol	12C05-N03	1
Fagron	Menthol	13D16-N090631/1300	1
Fagron	Menthol	16L20T04053177	1
Fagron	Menthol	1509045-03	1
Fagron	Menthol	12I19-N10	2
Fagron	Menthol	18G02T30	1
Fagron	Menthol	13016-N09	1
Fagron	Menthol	18G02-T30-062159	7
Fagron	Menthol	858607	1
Fagron	Menthol	18L04-T06-65445	1
Fagron	Menthol	1115262	1
Fargon/ Noweda	Menthol	13D16-N09	1
Fiebig	Menthol	1705022-01	1
Fiebig	Menthol	16095625	1
Fiebig	Menthol	17328803	1
Finteler Apotheke	Menthol	16095614	1
Finze	Menthol	9221710	1
Frey & Lau GmbH/Noweda	Menthol	1509045-03	2
Fagron	Menthol	16L20-T04	1
Frey*Lau GmbH	Menthol	1305010-01	1
Frey*Lau GmbH	Menthol	973192	1
Frey+Lau	Menthol	926636	1
Frey+Lau GmbH	Menthol	1509045-02	1
Frey+Lau GmbH	Menthol	1603024-01	1
frey+Lau/jenne	Menthol	1087209	1
Gehe	Menthol	12020411	1
Gehe	Menthol	13D16-N09	1
Gehe	Menthol	13377412	1
Gehe	Menthol	1502006-02	1
Gehe	Menthol	16095602	1
Gehe	Menthol	1705022-01	1
Gehe	Menthol	1802003-01	1
Gehe	Menthol	18128009	1
Gehe	Menthol	18G02-T30-062159	1
GEHE	Menthol	16L20-T04-044769	1
Gehe / Ensbona	Menthol	16L20-T04-044769	1
Gehe/ 27.10.12 EuRho	Menthol	11219216	1
Bombastus	Menthol	16L20-T04-053177	1
Euro OTC	Menthol	15-0904502	1
Fagron	Menthol	976035	1
Hedinger/Phönix	Menthol	17328802	1
Ichthyol / Phoenix	Menthol	16095603	1
Imhof	Menthol	15-5401	1
Jenne	Menthol	180200301	1
Kehr	Menthol	16095613	1

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Supplier	Substance	Batch	Spectra
Kehr	Menthol	16095620	1
Kehr	Menthol	1802003-01	1
Euro OTC	Menthol	1705022	1
L10	Menthol	1705022-01	1
L12	Menthol	1603024-01	1
L12	Menthol	1802003-01	1
L12	Menthol	1807044-01	1
Menthol/Phoenix	Menthol	16L20-T04-044769	1
Nachprüfung	Menthol	123456	1
Norex Flavours Pvt. Ltd...	Menthol	15286207	1
Norex Flavours Pvt. Ltd...	Menthol	15286205	2
Noweda	Menthol	1204036-01	1
Noweda	Menthol	1410004-01	1
Noweda	Menthol	15363809	1
Noweda	Menthol	1701014-02	1
Noweda	Menthol	17188904	1
Noweda	Menthol	1807044	1
Euro OTC	Menthol	858607	1
Euro OTC	Menthol	721123	1
Euro OTC	Menthol	16095614	1
Phoenix	Menthol	750137	1
Phoenix	Menthol	1403022-02	1
Phoenix	Menthol	16095617	1
Phoenix	Menthol	16095625	1
Phoenix	Menthol	3127	1
Phoenix	Menthol	1905013-01	1
Phoenix 15.04.2014	Menthol	12246211	1
Phoenix/Cealo	Menthol	1509045-01/4116F-018	1
Phonix	Menthol	1802003-01	1
phönix	Menthol	15363805	1
Phönix	Menthol	12246204	1
Phönix	Menthol	13159105	1
Phönix	Menthol	1608012-02	1
Phönix	Menthol	1807044-01	1
Phönix Gotha	Menthol	1410004-01	1
Caelo	Menthol	17188904	14
Retest	Menthol	1305010-02	1
Sanacorp	Menthol	1204036-01	1
Sanacorp	Menthol	1210017-01	1
Sanacorp	Menthol	13103901	1
Sanacorp	Menthol	1305010-01	1
Sanacorp	Menthol	6/AKD3	1
Sanacorp	Menthol	16095613	1
Sanacorp	Menthol	16095619	1
Sanacorp	Menthol	17328804	1
Caelo	Menthol	15076106	10
Sanacorp WE:02.09.16 ...	Menthol	15363809	1
Caelo	Menthol	1/AD1	1
Fagron	Menthol	15076101	1
siehe protokoll	Menthol	1008029-02	1
Spangro_12.03.2019	Menthol	1802003-01	1
VDL; 9.23EUR; 28.09.15	Menthol	15076113	1
WE:Sanacorp 03.11.2016 ...	Menthol	15363810	1
Caelo	Menthol		3
Caelo	Menthol	13377404	16
Euro OTC	Menthol	1403022-02	9
Euro OTC	Menthol	1509045	2
Fagron	Menthol	16L20-T04-044769	14
Fagron	Menthol	18L04-T06-065445	5

- 110 180 spectra from 742 *Apo-Ident* customers from a total of 31 635 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Menthol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Menthol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	364	1	110 324
Type B	0	456	19	118 667
Type C	0	1036	31	110 180

The substance/substance group *Menthol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	99.7260 % (> 98.9041 %)
Type B	100.0000 % (> 99.9893 %)	96.0000 % (> 95.3684 %)
Type C	100.0000 % (> 99.8899 %)	97.0947 % (> 96.8135 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Menthol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol hemihydrate	83.32	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Menthol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22657	22657	0.00	96.10
24690	22825	3.44	86.45
22825	22825	0.00	85.25
21443	24233	1.84	87.01
21601	21932	3.17	86.24
21932	21932	0.00	91.53
23596	22825	1.72	83.32
24233	24233	0.00	92.54

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Mepivacaine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20710-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mepivacaine hydrochloride; Mepivacaini hydrochloridum

Special notes

When selecting the *Mepivacaine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mepivacaine hydrochloride	2	2	5

Second-stage model

For differentiation of the substance/substance group *Mepivacaine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mepivacaine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Mepivacaine hydr...	12A20-N12	20710	40	1401555
Fagron	Mepivacaine hydr...	13L04-B07-297077	21672	60	AR-15-FG-007876-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 100 spectra of 2 reference samples from the substance/substance group *Mepivacaine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 589 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Mepivacaine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Mepivacaine hydrochloride	15I16-B01-322906	23212	40
Fagron	Mepivacaine hydrochloride	19F25-B02-365217	24950	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 5 batches from the substance/substance group *Mepivacaine hydrochloride*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Mepivacaine hydrochloride	13G05-N02	1
Fagron	Mepivacaine hydrochloride	13G05-N02	1
Fagron	Mepivacaine hydrochloride	13G05N02	1
Fagron	Mepivacaine hydrochloride	15I16-B01	1
Fagron	Mepivacaine hydrochloride	12E31-B40-305570	1
Fagron	Mepivacaine hydrochloride	12F20-N07	1

- 111 241 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mepivacaine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mepivacaine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	110 589
Type B	0	52	28	119 062
Type C	0	6	0	111 241

The substance/substance group *Mepivacaine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9893 %)	65.0000 % (> 61.2500 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mepivacaine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tretinoin	21.76	—
Methacholine chloride	34.98	—
Ornithine aspartate	40.80	—
Tetracaine base	42.99	—
Ibuprofen	47.73	—
Captopril	49.48	—
Ofloxacin	51.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mepivacaine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20710	20710	0.00	23.25
21672	21672	0.00	21.76

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Mesalazine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21772-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mesalazine; Mesalazinum

Special notes

When selecting the *Mesalazine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mesalazine	6	3	6

Second-stage model

For differentiation of the substance/substance group *Mesalazine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mesalazine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Mesalazine	1206029-04	21772	60	AR-15-FG-011819-01
Euro OTC	Mesalazine	1206029-04	21887	60	20140923
Euro OTC	Mesalazine	1602005	22518	40	20160218*
Euro OTC	Mesalazine	1602005-01	22925	40	20160218
Euro OTC	Mesalazine	1911016	25082	40	20191218*
Fagron	Mesalazine	15H13-B06-317177	22356	60	20150827
Fagron	Mesalazine	16I28-B02-327679	22929	40	20161128

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Mesalazine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 349 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Mesalazine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Mesalazine	1611019	22872	40
Euro OTC	Mesalazine	1902013	24477	40
Fagron	Mesalazine	17A17-B03-336444	23934	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 52 spectra from 10 *Apo-Ident* customers from 10 batches from the substance/substance group *Mesalazine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Mesalazine	18C30-B05-353048	1
Euro OTC	Mesalazine	1611019-03	2
Euro OTC	Mesalazine	1611019-01	2
Euro OTC	Mesalazine	1602005-02	7
Euro OTC	Mesalazine	1902013-01	6
Fagron	Mesalazine	18C30-B05-353048	4
Euro OTC	Mesalazine		1
Euro OTC	Mesalazine	1206029-04	1
Euro OTC	Mesalazine	1602005-01	3
Fagron	Mesalazine	16I28-B02-327679	24
Fagron	Mesalazine		1

- 111 195 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mesalazine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mesalazine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	120	0	119 022
Type C	0	48	4	111 195

The substance/substance group *Mesalazine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	92.3077 % (> 86.5385 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mesalazine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Miconazole nitrate	36.77	–
Midazolam hydrochloride	42.93	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mesalazine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21772	21772	0.00	42.40
21887	21772	7.53	45.53
22356	22518	3.31	55.92
22929	22518	5.24	53.96
22925	22518	1.31	58.76
25082	25082	0.00	61.15
22518	22518	0.00	58.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Metamizol sodium monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22634-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Metamizol sodium monohydrate; Metamizolum natricum monohydricum

Special notes

When selecting the *Metamizol sodium monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Metamizol sodium monohydrate	2	2	2

Second-stage model

For differentiation of the substance/substance group *Metamizol sodium monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Metamizol sodium monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Metamizol sodium...	161610	22634	40	20160714*
Caelo	Metamizol sodium...	15362816	22666	40	20151106

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 80 spectra of 2 reference samples from the substance/substance group *Metamizol sodium monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 609 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Metamizol sodium monohydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Metamizol sodium monohydrate	15362815	22726	40
Caelo	Metamizol sodium monohydrate	170584	23924	40
Caelo	Metamizol sodium monohydrate	161610	23313	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Metamizol sodium monohydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Metamizol sodium monohydrate	18026504	1
Caelo	Metamizol sodium monohydrate	17058404	2

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Metamizol sodium monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Metamizol sodium monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	110 609
Type B	0	120	0	119 022
Type C	0	3	0	111 244

The substance/substance group *Metamizol sodium monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Metamizol sodium monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ethyl hydrogen fumarate calcium	24.57	—
Fluocinolone acetonide, micronized	74.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Metamizol sodium monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22634	22634	0.00	71.46
22666	22634	2.88	71.51

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methacholine chloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20733-2020-07-14
Executing company HiperScan GmbH
 Weißeritzstraße 3
 01067 Dresden
 Germany

Relevant substance names

Methacholine chloride; Methacholinii chloridum

Special notes

When selecting the *Methacholine chloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methacholine chloride	7	3	20

Second-stage model

For differentiation of the substance/substance group *Methacholine chloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methacholine chloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Methacholine chl...	13260303	21251	40	20130827
Caelo	Methacholine chl...	13260303	21592	60	20130827
Caelo	Methacholine chl...	162293	22635	40	20160815*
Caelo	Methacholine chl...	16229304	22661	40	20160815
Caelo	Methacholine chl...	16229301	22662	40	20160815
Fagron	Methacholine chl...	12F01-N04	20733	60	1403251
Fagron	Methacholine chl...	16L20-B01-329966	22976	40	20170123
Fagron	Methacholine chl...	16L20-B01-329968	22977	40	20170123

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Methacholine chloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 600 spectra of 13 reference samples from the substance/substance group *Methacholine chloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Methacholine chloride	13260302	21420	60
Caelo	Methacholine chloride	163299	23049	40
Fagron	Methacholine chloride	17H03-B02-346564	24287	40
Caelo	Methacholine chloride	13260302	21420SI	60
Caelo	Methacholine chloride	13260302	21590	60
Caelo	Methacholine chloride	13260303	21592SI [†]	60
Caelo	Methacholine chloride	162293	22635SI [†]	40
Caelo	Methacholine chloride	16229304	22661SI [†]	40
Caelo	Methacholine chloride	16229301	22662SI [†]	40
Caelo	Methacholine chloride	163299	23049SI	40
Caelo	Methacholine chloride	163299	23624	40
Fagron	Methacholine chloride	16L20-B01-329966	22976SI [†]	40
Fagron	Methacholine chloride	16L20-B01-329968	22977SI [†]	40

- 118542 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 32 spectra from 16 *Apo-Ident* customers from 21 batches from the substance/substance group *Methacholine chloride*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
anzag 18.12.14 25,19	Methacholine chloride	14G30-B03-296209	1
Caelo	Methacholine chloride	16329901	2
Caelo	Methacholine chloride	17D13-B04-334377	1
Fagron	Methacholine chloride	14G30-B03-296210	1
Fagron	Methacholine chloride	10031504	1
Fagron	Methacholine chloride	24061503	1
Fagron	Methacholine chloride	15F10-B02-315831	1
Fagron	Methacholine chloride	15F10-B02-315523	1
Fagron	Methacholine chloride	312160	1
Fagron	Methacholine chloride	17D13-B04-334377	2
Fagron	Methacholine chloride	13121712	1
Fagron	Methacholine chloride	17D13-B04-334378	1
Fagron	Methacholine chloride	16L20-B01-329970	1
Fagron	Methacholine chloride	13/13-N03	2
Fagron	Methacholine chloride	16L20-B01	1
Fagron	Methacholine chloride	17H03-B02-346564	5

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Methacholine chloride	19H07-B04-365768	1
Fagron	Methacholine chloride	17D13-B04	1
Fagron	Methacholine chloride	14K20-B03-300973	2
Fagron	Methacholine chloride	13G10-N05	1
Fagron	Methacholine chloride	17H03-B02-346563	3
Phoenix/Cealo	Methacholine chloride	16L20-B01-329968	1

- 111 215 spectra from 742 *Apo-Ident* customers from a total of 31 870 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methacholine chloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methacholine chloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	582	18	118 542
Type C	0	31	1	111 215

The substance/substance group *Methacholine chloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	97.0000 % (> 96.5000 %)
Type C	100.0000 % (> 99.8899 %)	96.8750 % (> 87.5000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methacholine chloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxybuprocaine hydrochloride	46.54	—
Sildenafil citrate	51.76	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methacholine chloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20733	20733	0.00	72.77
21251	20733	5.56	75.85
22661	20733	6.55	78.39
22976	20733	4.22	70.22
22977	20733	6.56	77.55
21592	20733	7.39	71.36
22635	22635	0.00	85.92
22662	22635	6.93	83.79

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methionine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20971-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methionine; Methioninum

Special notes

When selecting the *Methionine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methionine	6	6	8

Second-stage model

For differentiation of the substance/substance group *Methionine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methionine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Methionine	15404102	22727	40	AR-17-FG-000285-02
Caelo	Methionine	16274007	23258	40	20161014
Euro OTC	Methionine	L1404041-01	21751	60	20140508
Euro OTC	Methionine	1602012	22368	60	20160219*
Fagron	Methionine	12K01-N03	20971	40	1402432
Fagron	Methionine	13L19-B36-295115	21786	60	20140108

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *Methionine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 389 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Methionine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Methionine	190211	24513	40
Euro OTC	Methionine	1609024	22787	40
Euro OTC	Methionine	1703042	23126	40
Euro OTC	Methionine	1710008	23777	40
Euro OTC	Methionine	1904012	24674	40
Euro OTC	Methionine	1909004	24851	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 10 spectra from 6 *Apo-Ident* customers from 8 batches from the substance/substance group *Methionine*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Methionine	16274009	1
Caelo	Methionine	17257501	2
Caelo	Methionine	17257502	2
Caelo	Methionine	18049105	1
Caelo	Methionine	16274002	1
Euro OTC	Methionine	1602012-01	1
Fagron	Methionine	13G09-N02	1
Fagron	Methionine	15A15-B08-307753	1

- 111 237 spectra from 742 *Apo-Ident* customers from a total of 31 883 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methionine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methionine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	240	0	118 902
Type C	0	10	0	111 237

The substance/substance group *Methionine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methionine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tretinoin	45.82	–
Ofloxacin	59.09	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methionine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22727	22727	0.00	47.40
23258	22727	2.52	47.74
20971	20971	0.00	84.06
21751	22368	3.37	82.02
21786	22368	4.38	83.38
22368	22368	0.00	80.95

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methoxsalen**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20233-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methoxsalen; Methoxsalenum

Special notes

When selecting the *Methoxsalen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methoxsalen	7	4	60

Second-stage model

For differentiation of the substance/substance group *Methoxsalen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methoxsalen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Methoxsalen	16103003	23167	40	20160415
Caelo	Methoxsalen	170781	23333	40	20170427*
Caelo	Methoxsalen	170781	23346	40	20170427*
Euro OTC	Methoxsalen	130604101	21555	60	20130805
Euro OTC	Methoxsalen	1506013	21862	60	20150706*
Euro OTC	Methoxsalen	1608019	22785	40	20160913*
Fagron	Methoxsalen	15J15-B03-321321	23165	40	20151124
Fagron	Methoxsalen	18A12-B50-355102	24697	40	20181112

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Methoxsalen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 470 spectra of 12 reference samples from the substance/substance group *Methoxsalen*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Methoxsalen	16103014	23166	40
Caelo	Methoxsalen	191960	24760	40
Euro OTC	Methoxsalen	1802021	24070	40
Euro OTC	Methoxsalen	1904009	24774	40
Caelo	Methoxsalen	16103014	23166SI	33
Caelo	Methoxsalen	16103003	23167SI [†]	37
Caelo	Methoxsalen	170781	23333SI [†]	40
Caelo	Methoxsalen	170781	23346SI [†]	36
Euro OTC	Methoxsalen	130604101	21555SI [†]	55
Euro OTC	Methoxsalen	1506013	21862SI [†]	45
Euro OTC	Methoxsalen	1608019	22785SI [†]	34
Fagron	Methoxsalen	15J15-B03-321321	23165SI [†]	30

- 118 672 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 188 spectra from 96 *Apo-Ident* customers from 64 batches from the substance/substance group *Methoxsalen*.
- Among them are spectra of independent samples from 60 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Methoxsalen	15244204	1
AHD	Methoxsalen	1608019-02	1
AHD	Methoxsalen	17078108	2
AHD	Methoxsalen	16103019	1
AHD	Methoxsalen	17078101	1
Anzag	Methoxsalen	1306041-01	1
Anzag	Methoxsalen	APHCFMPC16011M	1
Audor Pharma	Methoxsalen	AP15244213M	6
Audor Pharma	Methoxsalen	APHCFMPC16011M	6
Audor Pharma	Methoxsalen	15244213	1
Audor Pharma	Methoxsalen	AP1011024-01M	1
Audor Pharma	Methoxsalen	1203009M	1
Audor Pharma	Methoxsalen	APHCFMPC18003M	1
Caelo	Methoxsalen	11376413	2
Caelo	Methoxsalen	15099802	1
Caelo	Methoxsalen	15244204	3
Caelo	Methoxsalen	150613-01	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Methoxsalen	15244211	1
Caelo	Methoxsalen	1802021-01	3
Caelo	Methoxsalen	1608019-02	1
Caelo	Methoxsalen	16/079/M	1
Caelo	Methoxsalen	15244216	1
Caelo	Methoxsalen	11376420	1
Caelo	Methoxsalen	15244209	1
Caelo	Methoxsalen	17078108	1
Caelo	Methoxsalen	14F06-B05-296501	1
Caelo	Methoxsalen	1409003-01	5
Caelo	Methoxsalen	1409003-02	1
Caelo	Methoxsalen	11376433	1
Caelo	Methoxsalen	1503009-01	2
Caelo	Methoxsalen	15244205	2
Caelo	Methoxsalen	17078101	1
Caelo	Methoxsalen	1136428	1
EuRho	Methoxsalen	1104010-01	1
EuRho/Fiebig	Methoxsalen	1802021-01	1
Euro OTC	Methoxsalen	1203009-01	1
Euro OTC	Methoxsalen	140900302	1
Euro OTC	Methoxsalen	150300901	1
Euro OTC	Methoxsalen	1608019-02	8
Euro OTC	Methoxsalen	1104010-01	1
Euro OTC	Methoxsalen	1503009-02	8
Euro OTC	Methoxsalen	1306041-01	5
Euro OTC	Methoxsalen	120901501	1
Euro OTC	Methoxsalen	1608019-01	2
Euro OTC	Methoxsalen	1503009-01	11
Euro OTC	Methoxsalen	1506013-02	7
Euro OTC	Methoxsalen	1409003-02	2
Euro OTC	Methoxsalen	1802021-01	8
Euro OTC	Methoxsalen	1209015-01	4
Euro/Phönix	Methoxsalen	1608019-02	1
Euroo	Methoxsalen	1503009-01	1
Euro OTC	Methoxsalen	1506013-01	16
Fagron	Methoxsalen	11f21-n02	1
Fagron	Methoxsalen	11D07-N16	1
Fagron	Methoxsalen	12E02-N05	2
Fagron	Methoxsalen	12G02-N14	1
Fagron	Methoxsalen	14F06-B05-296500	1
Fagron	Methoxsalen	14F06-B05-301978	1
Fagron	Methoxsalen	15F23-B03-318166	5
Fagron	Methoxsalen	21111814	1
Fagron	Methoxsalen	15F23-B03-316262	1
Fagron	Methoxsalen	MS01/13-14	1
Fagron	Methoxsalen	11F21-N02	1
Fagron	Methoxsalen	15C10-B99-306266	1
Fagron	Methoxsalen	15F23-B03-309644	1
Fagron	Methoxsalen	2111A-03262	2
Fagron	Methoxsalen	15F23-B03	1
Fagron	Methoxsalen	14f06-b05-296500	1
Fagron	Methoxsalen	14F06-B05-296501	2
Herbal Creations	Methoxsalen	1608019-01	1
Herbal creations/Caesar...	Methoxsalen	15244208	1
Herbal creations/Caesar...	Methoxsalen	15244212	1
Herbal Creations/Caesar...	Methoxsalen	15244205	1
Herbal Creations/Caesar...	Methoxsalen	15244203	1
Nachprüfung	Methoxsalen	4211Q-03262	1
Noweda	Methoxsalen	11D07-N16	2
Noweda	Methoxsalen	140900302	1

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Supplier	Substance	Batch	Spectra
Noweda	Methoxsalen	19044103	1
Euro OTC	Methoxsalen	1409003-01	5
Phoenix	Methoxsalen	14F06-B05-296502	1
PHOENIX 18.02.14	Methoxsalen	1306041-01	2
Phönix	Methoxsalen	1608019-01	1
Euro OTC	Methoxsalen	160801902	1
Phytoceut.Ltd	Methoxsalen	1503009-01	3
Sanacorp	Methoxsalen	1AKD6	1
Say Phytoceut. Ltd	Methoxsalen	1209015-01	3
Euro OTC	Methoxsalen	1608019	1
Fagron	Methoxsalen	15J15-B03-321321	1

- 111 059 spectra from 742 *Apo-Ident* customers from a total of 31 827 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methoxsalen* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methoxsalen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	402	68	118 672
Type C	0	188	0	111 059

The substance/substance group *Methoxsalen* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	85.5319 % (> 84.8936 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 96.8085 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methoxsalen* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	61.23	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methoxsalen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21555	21862	4.86	69.37
21862	21862	0.00	68.82
22785	22785	0.00	69.39
23165	23333	4.31	67.20
23167	23333	2.39	64.61
23333	23333	0.00	64.45
23346	23346	0.00	61.26
24697	22785	5.96	69.22

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methyl-4-hydroxybenzoate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20345-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methyl-4-hydroxybenzoate; Methylis parahydroxybenzoas

Special notes

When selecting the *Methyl-4-hydroxybenzoate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methyl-4-hydroxybenzoate	6	9	89

Second-stage model

For differentiation of the substance/substance group *Methyl-4-hydroxybenzoate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methyl-4-hydroxybenzoate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Methyl-4-hydroxy...	11090034	20693	40	20110428
Caelo	Methyl-4-hydroxy...	181769	24223	40	20180824*
Euro OTC	Methyl-4-hydroxy...	1205025-01	20697	40	20120601
Euro OTC	Methyl-4-hydroxy...	1601037	22305	60	20160119*
Fagron	Methyl-4-hydroxy...	14L30-T01-018345	23223	40	20150309
Fagron	Methyl-4-hydroxy...	19B05-T03-062158	24588	40	20190228

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Methyl-4-hydroxybenzoate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 380 spectra of 9 reference samples from the substance/substance group *Methyl-4-hydroxybenzoate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Methyl-4-hydroxybenzoate	13268813	21439	60
Caelo	Methyl-4-hydroxybenzoate	15063820	23216	40
Caelo	Methyl-4-hydroxybenzoate	171581	23317	40
Caelo	Methyl-4-hydroxybenzoate	191302	24711	40
Caelo	Methyl-4-hydroxybenzoate	192334	24886	40
Euro OTC	Methyl-4-hydroxybenzoate	1706005	23703	40
Euro OTC	Methyl-4-hydroxybenzoate	1807009	24148	40
Euro OTC	Methyl-4-hydroxybenzoate	1902025	24568	40
Euro OTC	Methyl-4-hydroxybenzoate	1909009	24852	40

- 118 762 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 268 spectra from 197 *Apo-Ident* customers from 90 batches from the substance/substance group *Methyl-4-hydroxybenzoate*.
- Among them are spectra of independent samples from 89 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Methyl-4-hydroxybenzoate	12251624	1
AHD	Methyl-4-hydroxybenzoate	17343002	1
Anzag	Methyl-4-hydroxybenzoate	11345115	1
Fagron	Methyl-4-hydroxybenzoate	13B25-N03	2
Bombastus	Methyl-4-hydroxybenzoate	1212011-01	1
Caelo	Methyl-4-hydroxybenzoate	13268803	1
Caelo	Methyl-4-hydroxybenzoate	11090031	4
Caelo	Methyl-4-hydroxybenzoate	1108211930	1
Caelo	Methyl-4-hydroxybenzoate	11345115	7
Caelo	Methyl-4-hydroxybenzoate	9011303	1
Caelo	Methyl-4-hydroxybenzoate	11345120	2
Caelo	Methyl-4-hydroxybenzoate	713Q-01930	1
Caelo	Methyl-4-hydroxybenzoate	13081308	1
Caelo	Methyl-4-hydroxybenzoate	12251624	5
Caelo	Methyl-4-hydroxybenzoate	12251605	2
Caelo	Methyl-4-hydroxybenzoate	11090003	1
Caelo	Methyl-4-hydroxybenzoate	13268802	1
Caelo	Methyl-4-hydroxybenzoate	6091402	1
Caelo	Methyl-4-hydroxybenzoate	13268819	1
Caelo	Methyl-4-hydroxybenzoate	14120208	5
Caelo	Methyl-4-hydroxybenzoate	15063806	8
Caelo	Methyl-4-hydroxybenzoate	12081502	1
Caelo	Methyl-4-hydroxybenzoate	13268821	1
Caelo	Methyl-4-hydroxybenzoate	15063813	2
Caelo	Methyl-4-hydroxybenzoate	1601037-01	4
Caelo	Methyl-4-hydroxybenzoate	15063820	3
Caelo	Methyl-4-hydroxybenzoate	15444911	1
Caelo	Methyl-4-hydroxybenzoate	15444913	1
Caelo	Methyl-4-hydroxybenzoate	15444905	1

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Supplier	Substance	Batch	Spectra
Caelo	Methyl-4-hydroxybenzoate	16256104	2
Caelo	Methyl-4-hydroxybenzoate	16256118	5
Caelo	Methyl-4-hydroxybenzoate	17343002	7
Caelo	Methyl-4-hydroxybenzoate	1816903	1
Caelo	Methyl-4-hydroxybenzoate	18176903	7
Caelo	Methyl-4-hydroxybenzoate	17343010	1
Caelo	Methyl-4-hydroxybenzoate	15063818	3
Caelo	Methyl-4-hydroxybenzoate	15444916	1
Caelo	Methyl-4-hydroxybenzoate	13268815	1
Caelo	Methyl-4-hydroxybenzoate	19130205	1
Caelo	Methyl-4-hydroxybenzoate	13268813	7
Caelo	Methyl-4-hydroxybenzoate	16256115	2
Caelo	Methyl-4-hydroxybenzoate	15298102	12
Caelo	Methyl-4-hydroxybenzoate	11345103	1
Caelo	Methyl-4-hydroxybenzoate	12251619	1
Caelo	Methyl-4-hydroxybenzoate	13268809	5
Caelo	Methyl-4-hydroxybenzoate	16256103	3
Caelo	Methyl-4-hydroxybenzoate	12251611	1
Caelo	Methyl-4-hydroxybenzoate	15222203	4
Caelo	Methyl-4-hydroxybenzoate	17343013	6
Caelo	Methyl-4-hydroxybenzoate	18176910	3
Caelo	Methyl-4-hydroxybenzoate	15063819	4
Caelo	Methyl-4-hydroxybenzoate	17158101	17
Caelo	Methyl-4-hydroxybenzoate	13268804	9
Caelo	Methyl-4-hydroxybenzoate	111003301	1
Caelo	Methyl-4-hydroxybenzoate	1251624	1
Caelo	Methyl-4-hydroxybenzoate	15063803	1
Caelo	Methyl-4-hydroxybenzoate	15063802	6
Caelo	Methyl-4-hydroxybenzoate	15298101	1
Caesar & Loretz GmbH	Methyl-4-hydroxybenzoate	13268809	1
Caesar & Loretz GmbH	Methyl-4-hydroxybenzoate	18176903	1
Caesar & Loretz GmbH	Methyl-4-hydroxybenzoate	18176910	1
Caesar & Loretz GmbH/No...	Methyl-4-hydroxybenzoate	18176903	1
Caesar&Loretz	Methyl-4-hydroxybenzoate	17158101	1
Caesar&lorenz,Phoenix	Methyl-4-hydroxybenzoate	13268821	1
Caesar/Noweda	Methyl-4-hydroxybenzoate	15063806	1
Cealo/Gehe	Methyl-4-hydroxybenzoate	16256104	1
Eigenherstellung	Methyl-4-hydroxybenzoate	100912PML01	1
EuRho	Methyl-4-hydroxybenzoate	110403101	1
Euro OTC	Methyl-4-hydroxybenzoate	1009022-01	1
Euro OTC	Methyl-4-hydroxybenzoate	1212011-01	1
Euro OTC	Methyl-4-hydroxybenzoate	1401027-01	1
Euro OTC	Methyl-4-hydroxybenzoate	1406005-01	1
Euro OTC	Methyl-4-hydroxybenzoate	1758101	1
Euro OTC	Methyl-4-hydroxybenzoate	EA2781	1
Euro OTC	Methyl-4-hydroxybenzoate	1507042-01	10
Euro OTC	Methyl-4-hydroxybenzoate	280903701	2
Euro OTC	Methyl-4-hydroxybenzoate	1706005-02	1
Euro OTC	Methyl-4-hydroxybenzoate	172620	1
Euro OTC	Methyl-4-hydroxybenzoate	3115M-01930	1
Euro OTC	Methyl-4-hydroxybenzoate	140600501	1
Euro OTC	Methyl-4-hydroxybenzoate	1601037-01	4
Euro OTC	Methyl-4-hydroxybenzoate	1807009-01	7
Euro OTC	Methyl-4-hydroxybenzoate	1502009-01	9
Euro OTC	Methyl-4-hydroxybenzoate	1507042-02	2
Euro OTC	Methyl-4-hydroxybenzoate	1401027-02	2
Euro OTC	Methyl-4-hydroxybenzoate	2606022	1
Euro OTC	Methyl-4-hydroxybenzoate	4312I-01930	1
Euro OTC	Methyl-4-hydroxybenzoate	4314U-01930	1
Euro OTC	Methyl-4-hydroxybenzoate	1706005-01	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Methyl-4-hydroxybenzoate	1902025-01	1
Fagron	Methyl-4-hydroxybenzoate	12H02-N08	1
Fagron	Methyl-4-hydroxybenzoate	20111125-1	1
Fagron	Methyl-4-hydroxybenzoate	13E27-N09	1
Fagron	Methyl-4-hydroxybenzoate	12D18-N01	1
Fagron	Methyl-4-hydroxybenzoate	16256115	1
Gatt-Koller	Methyl-4-hydroxybenzoate	1803308	1
GATT-KOLLER/PHOENIX	Methyl-4-hydroxybenzoate	6112/01142814	1
Gehe	Methyl-4-hydroxybenzoate	11090031	1
Gehe	Methyl-4-hydroxybenzoate	11090020	1
Gehe	Methyl-4-hydroxybenzoate	17158101	1
Gehe	Methyl-4-hydroxybenzoate	1902025-01	1
Caelo	Methyl-4-hydroxybenzoate	15063819/1210217	1
Caelo	Methyl-4-hydroxybenzoate	11090030	1
Caelo	Methyl-4-hydroxybenzoate	290114PML01	1
L30	Methyl-4-hydroxybenzoate	17158101	2
Nachprüfung vom 31.12.2...	Methyl-4-hydroxybenzoate	12251624	2
Noweda	Methyl-4-hydroxybenzoate	17158101	1
Noweda	Methyl-4-hydroxybenzoate	16256118	1
Phoenix	Methyl-4-hydroxybenzoate	1706005-01	1
Phoenix	Methyl-4-hydroxybenzoate	18176910	1
Phönix	Methyl-4-hydroxybenzoate	2AKD3	1
Phönix	Methyl-4-hydroxybenzoate	17343010	1
Phönix	Methyl-4-hydroxybenzoate	1807009-01	1
PHÖNIX	Methyl-4-hydroxybenzoate	15063819	1
Phönix 14.01.2014	Methyl-4-hydroxybenzoate	12251624	1
phönix 4.12.2013	Methyl-4-hydroxybenzoate	1212011/01	1
Sanacorp E.K :2,76 - ...	Methyl-4-hydroxybenzoate	13268804	1
Fagron	Methyl-4-hydroxybenzoate		1

- 110 979 spectra from 742 *Apo-Ident* customers from a total of 31 803 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methyl-4-hydroxybenzoate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methyl-4-hydroxybenzoate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	380	0	118 762
Type C	0	266	2	110 979

The substance/substance group *Methyl-4-hydroxybenzoate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.4211 %)
Type C	100.0000 % (> 99.8899 %)	99.2537 % (> 98.1343 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methyl-4-hydroxybenzoate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	27.22	—
Chloramphenicol	37.63	—
Levothyroxin sodium	42.13	—
Oxytetracycline hydrochloride	49.05	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methyl-4-hydroxybenzoate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20693	24223	5.62	54.57
20697	24223	5.63	54.41
22305	22305	0.00	53.09
23223	22305	7.27	52.28
24223	24223	0.00	54.07
24588	22305	9.91	51.59

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methylcellulose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20705-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methylcellulose; Hydroxypropylcellulose (300 mPa · s); Hydroxypropylcellulosum (300 mPa · s); Hypromellose 4000; Hypromellose E4M Prem; Methylcellulosum

Special notes

When selecting the *Methylcellulose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Hydroxypropylcellulose (300 mPa · s)	4	2	6
Hypromellose 4000	4	3	108
Methylcellulose	4	2	39

Second-stage model

For differentiation of the substance/substance group *Methylcellulose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methylcellulose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Hydroxypropylcel...	12093107	20686	40	1402049
Caelo	Hydroxypropylcel...	14189804	21767	60	AR-15-FG-014922-01
Caelo	Hydroxypropylcel...	15345001	22258	60	20151104
Caelo	Hydroxypropylcel...	181146	24249	40	20180618*
Caelo	Hypromellose 4000	13155006	20919	40	1402056
Caelo	Hypromellose 4000	13155006	20931	40	20130529
Caelo	Hypromellose 4000	14338801	21702	45	20141217
Fagron	Hypromellose 4000	15G08-B14-314845	22609	40	20150727
Fagron	Hypromellose 4000	19G17-B04-194255	25060	40	20190830
Caelo	Methylcellulose	13130115	21570	60	20130517
Caelo	Methylcellulose	160602	22457	60	20160323*
Fagron	Methylcellulose	12D02-N09	20705	40	1402447
Fagron	Methylcellulose	15H04-B07-331291	23224	40	20150824

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 605 spectra of 13 reference samples from the substance/substance group *Methylcellulose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 110 084 spectra from a total of 1954 batches from further 388 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Methylcellulose*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hydroxypropylcellulose (300 ...	15345009	23123	40
Caelo	Hydroxypropylcellulose (300 ...	17355801	23974	40
Caelo	Hypromellose 4000	162244	22757	40
Caelo	Hypromellose 4000	171150	23284	40
Caelo	Hypromellose 4000	190696	24516	40
Caelo	Methylcellulose	171704	23627	40
Caelo	Methylcellulose	183318	24560	40

- 118862 spectra from a total of 2413 batches from further 797 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 498 spectra from 261 *Apo-Ident* customers from 162 batches from the substance/substance group *Methylcellulose*.
- Among them are spectra of independent samples from 152 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Hydroxypropylcellulose (300 ...	13031309	1
Caelo	Hydroxypropylcellulose (300 ...	14189801	2
Caelo	Hydroxypropylcellulose (300 ...	15129707	1
Caelo	Hydroxypropylcellulose (300 ...	15345008	1
Noweda	Hydroxypropylcellulose (300 ...	18114605	1
Caelo	Hydroxypropylcellulose (300 ...	13031306	1
AHD	Hypromellose 4000	16H23-B02-325994	1
Fagron	Hypromellose 4000	12D03-N03	1
Alliance Health 27.12.2...	Hypromellose 4000	13D03-N03	1
Caelo	Hypromellose 4000	12098702	1
Caelo	Hypromellose 4000	12215504	2
Caelo	Hypromellose 4000	12215505	1
Caelo	Hypromellose 4000	13155004	10
Caelo	Hypromellose 4000	13155002	1
Caelo	Hypromellose 4000	12239502	1
Caelo	Hypromellose 4000	14C05-B03-294708	1
Caelo	Hypromellose 4000	14338802	1
Caelo	Hypromellose 4000	15G08-B14-314845	3
Caelo	Hypromellose 4000	16224403	13
Caelo	Hypromellose 4000	16224407	11

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Supplier	Substance	Batch	Spectra
Caelo	Hypromellose 4000	16224409	8
Caelo	Hypromellose 4000	16224408	1
Caelo	Hypromellose 4000	171150085501	1
Caelo	Hypromellose 4000	17115008	8
Caelo	Hypromellose 4000	17132101	1
Caelo	Hypromellose 4000	5121818	1
Caelo	Hypromellose 4000	18132111	3
Caelo	Hypromellose 4000	13d03-n03	1
Caelo	Hypromellose 4000	18132105	11
Caelo	Hypromellose 4000	18132109	4
Caelo	Hypromellose 4000	16B16-B07-321327	2
Caelo	Hypromellose 4000	18132102	4
Caelo	Hypromellose 4000	18132106	2
Caelo	Hypromellose 4000	16224406	3
Caelo	Hypromellose 4000	18D04-B03-355144	1
Caelo	Hypromellose 4000	17115005	17
Caelo	Hypromellose 4000	15G08-B14-310845	1
Caelo	Hypromellose 4000	16224401	6
Caelo	Hypromellose 4000	180215H/17115004	1
Caelo	Hypromellose 4000	19069608	2
Caelo	Hypromellose 4000	15B02-B05-308852	1
Caelo	Hypromellose 4000	13100304	2
Caelo	Hypromellose 4000	17115004	2
Caelo	Hypromellose 4000	18132101	10
Caelo	Hypromellose 4000	19069601	6
Caesar & Loretz GmbH	Hypromellose 4000	18132109	1
Caesar & Loretz GmbH	Hypromellose 4000	18132111	1
Caesar & Loretz GmbH	Hypromellose 4000	18132105	1
Caesar & Loretz GmbH / ...	Hypromellose 4000	16224403	1
Caelo	Hypromellose 4000	19069609	1
Caesar & Loretz GmbH/No...	Hypromellose 4000	19069601	1
Cealo/Gehe	Hypromellose 4000	18132101	1
DOW Chemical Company Mi...	Hypromellose 4000	14G02-B11-296850	1
Euro OTC	Hypromellose 4000	18132105	1
Fagron	Hypromellose 4000	12A30-N02	3
Fagron	Hypromellose 4000	20110612-2	1
Fagron	Hypromellose 4000	10G09-N03	1
Fagron	Hypromellose 4000	12E02-N03	3
Fagron	Hypromellose 4000	12G23-N03	1
Fagron	Hypromellose 4000	1A01012N11	1
Fagron	Hypromellose 4000	14C05-B03	1
Fagron	Hypromellose 4000	13D03N03	1
Fagron	Hypromellose 4000	1K01012N11	1
Fagron	Hypromellose 4000	14C05-B03-294708	4
Fagron	Hypromellose 4000	14C05-B03-294711	1
Fagron	Hypromellose 4000	14G02-B11-296851	1
Fagron	Hypromellose 4000	14C05B03	1
Fagron	Hypromellose 4000	14G02-B11-296850	5
Fagron	Hypromellose 4000	14C-05B03	1
Fagron	Hypromellose 4000	14G02-B11	3
Fagron	Hypromellose 4000	14G02-B11-302119	1
Fagron	Hypromellose 4000	15B02-B05	1
Fagron	Hypromellose 4000	15B02-B05-308852	1
Fagron	Hypromellose 4000	3G08012N11	1
Fagron	Hypromellose 4000	15G08-B14	1
Fagron	Hypromellose 4000	16B16-B07-318276	2
Fagron	Hypromellose 4000	16B16-B07-321327	2
Fagron	Hypromellose 4000	16B-16-B07-321327	1
Fagron	Hypromellose 4000	16B16-B07-321579	1
Fagron	Hypromellose 4000	16H23-B02-332066	6

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Supplier	Substance	Batch	Spectra
Fagron	Hypromellose 4000	18D04-B03	3
Fagron	Hypromellose 4000	349970	1
Fagron	Hypromellose 4000	18A17-B04	2
Fagron	Hypromellose 4000	D180HBA012	1
Fagron	Hypromellose 4000	D180J45013	1
Fagron	Hypromellose 4000	18D04-B03-35144	1
Fagron	Hypromellose 4000	17115005	1
Fagron	Hypromellose 4000	2H12012N12	1
Fagron	Hypromellose 4000	14G02-B11-302118	6
Fagron	Hypromellose 4000	YI16012N11	1
Fagron	Hypromellose 4000	13h09-m04	1
Fagron	Hypromellose 4000	16B16-B07-325280	5
Fagron	Hypromellose 4000	18D04-B03-350745	1
Fagron	Hypromellose 4000	14G02-B11-302121	1
Fagron	Hypromellose 4000	13D03-N03	7
Fagron	Hypromellose 4000	ZH19012N12	1
Fagron	Hypromellose 4000	18A17-B04-345100	2
Fagron	Hypromellose 4000	16B16-B07-321328	1
Fagron	Hypromellose 4000	12H20-N05	1
Fagron	Hypromellose 4000	13E02-B03-290532	1
Fagron	Hypromellose 4000	700182-0001	2
Fagron	Hypromellose 4000	14g02-b11-302118	2
Fagron	Hypromellose 4000	15g08-b14-314845	1
Fagron	Hypromellose 4000	16B16-B07-323114	3
Fagron	Hypromellose 4000	15G08B14314185	2
Fagron	Hypromellose 4000	16B16_B07	1
Fagron	Hypromellose 4000	325994	1
Fagron	Hypromellose 4000	18A17-B04-346208	1
Fagron	Hypromellose 4000	D180F8Q011	1
Fagron	Hypromellose 4000	16B16-B07_321327	1
Fagron	Hypromellose 4000	16H23B-02	1
Fagron	Hypromellose 4000	18D04-B03-348465	4
Fagron	Hypromellose 4000	18D04-B03-355144	2
Fagron	Hypromellose 4000	18D04-B03-352349	1
Fagron	Hypromellose 4000	1J31012N11	3
Fagron	Hypromellose 4000	15G08-B14-310845	8
Fagron	Hypromellose 4000	16B16-B07-318531	8
Fagron	Hypromellose 4000	12G23-N03	1
Fagron	Hypromellose 4000	13H09-N04	9
Fragon/Phoenix	Hypromellose 4000	18D04-b03-349970	1
FRAGON/Poenix	Hypromellose 4000	16B16-B07-18276	1
Gatt-Koller / Phoenix	Hypromellose 4000	14C05-B03-291647	2
Gehe	Hypromellose 4000	14G02-B11	1
Gehe	Hypromellose 4000	19069601	1
GEHE	Hypromellose 4000	17115008	1
GEHE	Hypromellose 4000	16H23-B02	1
GEHE	Hypromellose 4000	18A17-B04	3
GEHE	Hypromellose 4000	18049201	1
Gehe / 26.10.12 Fragon	Hypromellose 4000	9D30-N05	1
Caelo	Hypromellose 4000	D180F8Q011	1
Caelo	Hypromellose 4000	16224404	1
Fagron	Hypromellose 4000	14c05-B03-294708	1
Jenne	Hypromellose 4000	15G08-B14	1
Jenne	Hypromellose 4000	18D04-B03-350745	1
Kehr	Hypromellose 4000	17115005	1
L12	Hypromellose 4000	16224406	1
L12	Hypromellose 4000	17115008	1
Nachprüfung 2609	Hypromellose 4000	11H26-N01	1
Noweda	Hypromellose 4000	1315505	1
Noweda	Hypromellose 4000	18132111	1

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Supplier	Substance	Batch	Spectra
Fagron	Hypromellose 4000	15g08-b14-310845	2
Phoenix	Hypromellose 4000	13E02-B03	1
Phoenix	Hypromellose 4000	14c05-b03-294708	1
Phoenix	Hypromellose 4000	16B16-B07	2
Phoenix	Hypromellose 4000	16224407	1
Phoenix	Hypromellose 4000	16B16-B07-321327	1
Phonix	Hypromellose 4000	13H09-N04	1
Phönix	Hypromellose 4000	16224403	1
PHÖNIX	Hypromellose 4000	16H23-B02-325994	1
Phönix Gotha	Hypromellose 4000	14G02-B11-296850	1
Fagron	Hypromellose 4000	18D04-B03-352746	2
Fagron	Methylcellulose	131301 (09)	1
Caelo	Methylcellulose	12044931	2
Caelo	Methylcellulose	10247604	1
Caelo	Methylcellulose	12044907	1
Caelo	Methylcellulose	12044918	2
Caelo	Methylcellulose	12044927	6
Caelo	Methylcellulose	13021401	1
Caelo	Methylcellulose	20021401	1
Caelo	Methylcellulose	5081404	1
Caelo	Methylcellulose	14197502	6
Caelo	Methylcellulose	16060206	12
Caelo	Methylcellulose	16060210	10
Caelo	Methylcellulose	16060202	1
Caelo	Methylcellulose	16284003	6
Caelo	Methylcellulose	16284004	1
Caelo	Methylcellulose	17170404	1
Caelo	Methylcellulose	18045101	5
Caelo	Methylcellulose	1628404	1
Caelo	Methylcellulose	14197514	7
Caelo	Methylcellulose	18331803	4
Caelo	Methylcellulose	12044917	1
Caelo	Methylcellulose	15179605	7
Caelo	Methylcellulose	16284006	6
Caelo	Methylcellulose	18045107	1
Caelo	Methylcellulose	14197513	1
Caelo	Methylcellulose	13130121	3
Caelo	Methylcellulose	18045114	2
Caelo	Methylcellulose	13130104	5
Caelo	Methylcellulose	12044922	2
Caelo	Methylcellulose	17170405	4
Caelo	Methylcellulose	15179602	11
Caelo	Methylcellulose	13130109	5
Caesar & Loretz GmbH	Methylcellulose	12044922	1
Caesar & Loretz GmbH	Methylcellulose	18331803	1
Caesar & Loretz GmbH / ...	Methylcellulose	18331803	1
Euro OTC	Methylcellulose	10247609	1
Euro OTC	Methylcellulose	16284003	1
Euro OTC	Methylcellulose	15179602	1
Fagron	Methylcellulose	12H06-N06	2
Fagron	Methylcellulose	13E02-B03-290531	3
Fagron	Methylcellulose	13/26-N04	1
Fagron	Methylcellulose	15G08B14314845	1
Fiebig	Methylcellulose	18045101	1
Gatt-Koller	Methylcellulose	18045107	1
Gehe	Methylcellulose	16284003	1
L12	Methylcellulose	16284003	1
L12	Methylcellulose	17170405	1
Phoenix	Methylcellulose	18331803	1
Phoenix/Cealo	Methylcellulose	17170404	1

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Supplier	Substance	Batch	Spectra
Bombastus	Methylcellulose	17170405	1
Sanacorp	Methylcellulose	1717405	1
Sanacorp	Methylcellulose	18331803	1
Caelo	Methylcellulose	12044903	2
Caelo	Hydroxypropylcellulose (300 ...	15345001	2
Caelo	Hypromellose 4000	14338801	3
Fagron	Hypromellose 4000	15G08-B14-314845	6
Caelo	Methylcellulose	13130115	6

- 110 749 spectra from 742 *Apo-Ident* customers from a total of 31 731 batches from a further 704 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methylcellulose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methylcellulose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	605	0	110 084
Type B	0	260	20	118 862
Type C	0	490	8	110 749

The substance/substance group *Methylcellulose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0083 %)
Type B	100.0000 % (> 99.9893 %)	92.8571 % (> 91.7857 %)
Type C	100.0000 % (> 99.8899 %)	98.3936 % (> 97.7912 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methylcellulose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol valerate	34.10	—
Hydrocortisone	35.72	—
Menthol	46.67	—
Calcium citrate tetrahydrate	56.87	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methylcellulose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20705	20705	0.00	60.11
21570	20705	8.02	62.69
22457	22457	0.00	59.92
23224	20705	5.14	59.50
21767	21767	0.00	45.92
22609	20705	10.36	57.45
20919	20919	0.00	49.60
20931	20919	2.27	50.91
21702	20919	9.23	47.61
25060	20919	18.82	48.67
20686	20686	0.00	44.95
24249	24249	0.00	49.69
22258	21767	9.06	46.07

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methylcobalamin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20743-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methylcobalamin

Special notes

When selecting the *Methylcobalamin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methylcobalamin	9	1	3

Second-stage model

For differentiation of the substance/substance group *Methylcobalamin* the following second-stage model is used:

- [Submodel 4](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methylcobalamin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Methylcobalamin	1207019-01	20743	40	1402501
Euro OTC	Methylcobalamin	1401032-01	21721	60	8778
Euro OTC	Methylcobalamin	1510002	22234	60	20151201*
Euro OTC	Methylcobalamin	1401032	22239	60	20151201*
Euro OTC	Methylcobalamin	1601043	22379	60	20160209*
Euro OTC	Methylcobalamin	1804006	24072	40	20180420*
Euro OTC	Methylcobalamin	1809001	24311	40	20180925*
Euro OTC	Methylcobalamin	1904002	24775	40	20190806*
Euro OTC	Methylcobalamin	2002014	25135	40	20200401*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 9 reference samples from the substance/substance group *Methylcobalamin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 249 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 40 spectra of 1 reference samples from the substance/substance group *Methylcobalamin*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Methylcobalamin	1711031	23885	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Methylcobalamin*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Methylcobalamin	1711031-01	1
Euro OTC	Methylcobalamin	1804006-01	1
Euro OTC	Methylcobalamin	1601043-02	1

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methylcobalamin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methylcobalamin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	110 249
Type B	0	40	0	119 102
Type C	0	3	0	111 244

The substance/substance group *Methylcobalamin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methylcobalamin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cyanocobalamin	10.22	9.36
Bacitracin	14.12	23.94
Capsaicin	26.37	—
Ethinylestradiol	32.47	226.09
Calcium citrate tetrahydrate	33.94	84.99
Prednisolon dihydrogen phosphate dinat...	35.71	—
Prednisone	36.41	—
Magnesium citrate	38.79	—
Minoxidil	39.26	—
Estradiol hemihydrate	40.53	—
Polymyxin B sulfate	44.29	—
L-glutathione	44.43	—
Glycyrrhizic acid	44.54	—
Levothyroxin sodium	46.95	—
Gelatine, white	47.36	—
Escin, water-soluble	47.84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methylcobalamin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24311	24311	0.00	14.85
25135	25135	0.00	15.95
24775	24775	0.00	15.06

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22234	22234	0.00	14.12
22379	22379	0.00	17.84
21721	21721	0.00	26.37
20743	20743	0.00	22.83
22239	22239	0.00	22.42
24072	24072	0.00	15.77

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Methylprednisolone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20953-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Methylprednisolone; Methylprednisolonum

Special notes

When selecting the *Methylprednisolone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Methylprednisolone	3	3	2

Second-stage model

For differentiation of the substance/substance group *Methylprednisolone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Methylprednisolone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Methylprednisolone	13G19-N05	20953	40	1402438
Fagron	Methylprednisolone	15I04-B05-311572	22275	45	AR-16-FG-009102-01
Fagron	Methylprednisolone	15I04-B05-311572	22275SI	45	AR-16-FG-009102-01
Fagron	Methylprednisolone	15I04-B05-311572	22354	45	20151026
Fagron	Methylprednisolone	15I04-B05-311572	22354SI	45	20151026
Fagron	Methylprednisolone	18E16-B02-B02-358166	24572	40	20180611

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Methylprednisolone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 429 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 230 spectra of 6 reference samples from the substance/substance group *Methylprednisolone*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Methylprednisolone	12D17-N04	20650	40
Fagron	Methylprednisolone	15L15-B01-321887	23229	40
Fagron	Methylprednisolone	18A03-B05-345742	23997	40
Fagron	Methylprednisolone	15L15-B01-321887	23229SI	30
Fagron	Methylprednisolone	18A03-B05-345742	23997SI	40
Fagron	Methylprednisolone	18E16-B02-B02-358166	24572SI [†]	40

- 118912 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Methylprednisolone*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Methylprednisolone	12D17-N04	1
Fagron	Methylprednisolone	18A03-B05	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Methylprednisolone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Methylprednisolone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	230	0	118 912
Type C	0	1	1	111 245

The substance/substance group *Methylprednisolone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.3913 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Methylprednisolone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisolon dihydrogen phosphate dinat...	24.20	—
Cyanocobalamin	29.02	—
Triamcinolone, micronized	32.36	—
Bacitracin	38.29	—
Magnesium citrate	48.41	—
Prednisone	50.83	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Methylprednisolone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22275	22275	0.00	30.73
24572	22275	4.89	29.65
22354	22275	2.07	30.55
20953	20953	0.00	24.20

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Metoclopramide hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21662-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Metoclopramide hydrochloride; Metoclopramidi hydrochloridum

Special notes

When selecting the *Metoclopramide hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Metoclopramide hydrochloride	3	1	3

Second-stage model

For differentiation of the substance/substance group *Metoclopramide hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Metoclopramide hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Metoclopramide h...	14193102	21662	60	AR-15-FG-002889-01
Caelo	Metoclopramide h...	14193102	21746	60	20140725
Caelo	Metoclopramide h...	15421101	23234	40	20160226
Gatt-Koller	Metoclopramide h...	20170236	24410	40	20170724

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Metoclopramide hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 489 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Metoclopramide hydrochloride*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Metoclopramide hydrochloride	15421102	23718	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH, Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 19 spectra from 19 *Apo-Ident* customers from 3 batches from the substance/substance group *Metoclopramide hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Metoclopramide hydrochloride	14193101	1
Caelo	Metoclopramide hydrochloride	15227001	16
Caelo	Metoclopramide hydrochloride	3414U-018969	1
Caesar&lloretz,Phoenix	Metoclopramide hydrochloride	14193101	1

- 111 228 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Metoclopramide hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Metoclopramide hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	40	0	119 102
Type C	0	19	0	111 228

The substance/substance group *Metoclopramide hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Metoclopramide hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methylprednisolone	59.03	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Metoclopramide hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21662	21662	0.00	59.03
21746	21662	3.69	59.88
23234	21662	5.57	59.74
24410	21662	4.83	60.88

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Metoprolol tartrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21753-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Metoprolol tartrate; Metoprololi tartras

Special notes

When selecting the *Metoprolol tartrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Metoprolol tartrate	6	2	27

Second-stage model

For differentiation of the substance/substance group *Metoprolol tartrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Metoprolol tartrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Metoprolol tartr...	APMTP02218MT	24596	40	20190220
Euro OTC	Metoprolol tartr...	2001021	25098	40	20200116*
Fagron	Metoprolol tartr...	16E31-B03-327107	22927	40	20160627
Fagron	Metoprolol tartr...	16E31-B03-327107	22943	40	20160627
Fagron	Metoprolol tartr...	16E31-B03-327107	22944	40	20160627
Fagron	Metoprolol tartr...	19K20-F03-366934	25061	40	20191218
Inresa	Metoprolol tartr...	309905RII	21753	60	AR-15-FG-006635-01
Inresa	Metoprolol tartr...	405005RII	21805	60	20140430

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Metoprolol tartrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 329 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Metoprolol tartrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Metoprolol tartrate	18K26-B01-359370	24825	40
Inresa	Metoprolol tartrate	405005RIIC	22908	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 78 spectra from 44 *Apo-Ident* customers from 30 batches from the substance/substance group *Metoprolol tartrate*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Metoprolol tartrate	18K26-B01-359371	1
Andor	Metoprolol tartrate	APMTP0117MT	1
Antares	Metoprolol tartrate	1014Q-07308	1
Apomix/Gehe	Metoprolol tartrate	18K26-B01-355911	1
Audor Pharma	Metoprolol tartrate	APMTP00117MT	13
Audor Pharma	Metoprolol tartrate	MTP00117MT	1
Caelo	Metoprolol tartrate	APMT00117MT	1
Caelo	Metoprolol tartrate	17G03-B09-351672	1
Fagro	Metoprolol tartrate	16MD000095	1
Fagron	Metoprolol tartrate	17G03-B09-351672	1
Fagron	Metoprolol tartrate	18K26-B01-362451	1
Fagron	Metoprolol tartrate	17G03-B09-347089	1
Fagron	Metoprolol tartrate	1700305RII	1
Fagron	Metoprolol tartrate	17G03-B09-350669	2
Fagron	Metoprolol tartrate	17G03-B03-353935	1
Fagron	Metoprolol tartrate	18K26-B01-359370	1
Fagron	Metoprolol tartrate	18K26-B01-355911	2
Fagron	Metoprolol tartrate	17G03-B09-340197	2
Audor Pharma	Metoprolol tartrate	APMTP0C117MT	1
HELIOS Klinikum Erfurt/...	Metoprolol tartrate	405005RIIC	1
Inresa	Metoprolol tartrate	4050005RIIB	1
Inresa	Metoprolol tartrate	504005RIIC/29082016	1
Klosterring	Metoprolol tartrate	17G03-B09-345301	1
Audor Pharma	Metoprolol tartrate	MTP02218	1
Sidonia	Metoprolol tartrate	405005RIIC/09062017	1
Sigma Adrich/Alliance H.	Metoprolol tartrate	PHR1076	1
Sigma-Aldrich GmbH	Metoprolol tartrate	LRAA6905	4
Th. Geyer	Metoprolol tartrate	56392-17-7	1
Fagron	Metoprolol tartrate	16E31-B03-325535	1
Audor Pharma	Metoprolol tartrate	APMTP02218MT	7
Fagron	Metoprolol tartrate	16E31-B03-327107	23
	Metoprolol tartrate		1

- 111 169 spectra from 742 *Apo-Ident* customers from a total of 31 862 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Metoprolol tartrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Metoprolol tartrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	80	0	119 062
Type C	0	78	0	111 169

The substance/substance group *Metoprolol tartrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 92.3077 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Metoprolol tartrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tetracaine base	44.49	—
Ibuprofen	49.54	—
Omeprazole	56.65	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Metoprolol tartrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22944	25098	4.28	62.77
25098	25098	0.00	62.32
21753	21753	0.00	64.06
21805	21753	3.63	64.46
22927	21753	6.72	59.13
22943	21753	3.43	63.19
25061	21753	6.94	59.90
24596	25098	5.03	60.90

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Metronidazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20001-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Metronidazole; Metronidazolium

Special notes

When selecting the *Metronidazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Metronidazole	7	14	493

Second-stage model

For differentiation of the substance/substance group *Metronidazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Metronidazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Metronidazole	12110410	20857	40	20120515
Caelo	Metronidazole	13095007	21356	40	20130426
Caelo	Metronidazole	13095007	21360	40	20130426
Caelo	Metronidazole	160892	22472	60	20160413*
Euro OTC	Metronidazole	1212030-02	21213	40	20130627
Euro OTC	Metronidazole	1508004	21881	60	20150819*
Fagron	Metronidazole	13D10-N02	21212	40	20130516
Fagron	Metronidazole	16I19-B04-326155	22835	40	20161013

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Metronidazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 540 spectra of 14 reference samples from the substance/substance group *Metronidazole*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Metronidazole	13095005	21214	40
Caelo	Metronidazole	172905	23808	40
Caelo	Metronidazole	190102	24558	40
Euro OTC	Metronidazole	1609028	22751	40
Euro OTC	Metronidazole	1612013	22917	40
Euro OTC	Metronidazole	1701039	23132	40
Euro OTC	Metronidazole	1707008	23542	30
Euro OTC	Metronidazole	1706022	23550	30
Euro OTC	Metronidazole	1802007	23946	40
Euro OTC	Metronidazole	1807039	24203	40
Euro OTC	Metronidazole	1901042	24449	40
Euro OTC	Metronidazole	1906012	24766	40
Euro OTC	Metronidazole	1908028	24864	40
Fagron	Metronidazole	17C10-B04-355868	24586	40

- 118 602 spectra from a total of 2406 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2468 spectra from 611 *Apo-Ident* customers from 524 batches from the substance/substance group *Metronidazole*.
- Among them are spectra of independent samples from 490 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
17270001	Metronidazole	17058026	1
A.H. 19.02.13 ek: 5,86EUR	Metronidazole	12G04-N15	1
AHD	Metronidazole	15253005	1
AHD	Metronidazole	16I19-B04-329160	1
AHD	Metronidazole	17290518	1
Fagron	Metronidazole	13/21-N7	2
AHD 03.02.17	Metronidazole	16089212	1
ALH	Metronidazole	1609028-01	1
Alliance	Metronidazole	12339502	1
Alliance Health 20.05.2...	Metronidazole	1307042-01	2
Alliance Health 23.01.2...	Metronidazole	1212001-02	1
Alliance Healthcare	Metronidazole	12110415	1
anzag	Metronidazole	14C14-B02-291276	2
Anzag	Metronidazole	11373512	1
Anzag	Metronidazole	1505024-01	1
Anzag	Metronidazole	15253022	1
Anzag 21.10.14 EK 2.85	Metronidazole	13095007	1
Caelo	Metronidazole	17058026	14
Caelo	Metronidazole	11319824	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Anzag;14,21EUR;16.04.15	Metronidazole	13214012	1
Apoident,Phönix, 09.11...	Metronidazole	1701039-01	1
Apotheke an der Bornhei...	Metronidazole	16089223	1
Bombastus	Metronidazole	13214018	1
Bombastus	Metronidazole	123Validierung	1
Bombastus	Metronidazole	1609028-01	1
Bombastus	Metronidazole	15253032	1
Bombastus	Metronidazole	16089220	1
Bombastus	Metronidazole	18026401	1
Caelo	Metronidazole	12339519	12
Caelo	Metronidazole	11319812	1
Caelo	Metronidazole	28061204	1
Caelo	Metronidazole	10368313	1
Caelo	Metronidazole	607211870	1
Caelo	Metronidazole	11319819	1
Caelo	Metronidazole	11319825	3
Caelo	Metronidazole	12110414	3
Caelo	Metronidazole	3112M-01870	1
Caelo	Metronidazole	15121202	1
Caelo	Metronidazole	20140612-12	1
Caelo	Metronidazole	102311870	1
Caelo	Metronidazole	12L17-N11	3
Caelo	Metronidazole	12110411	5
Caelo	Metronidazole	1109030-01	2
Caelo	Metronidazole	12110421	6
Caelo	Metronidazole	12110105	1
Caelo	Metronidazole	12339501	7
Caelo	Metronidazole	12339503	6
Caelo	Metronidazole	12110423	1
Caelo	Metronidazole	1239504	1
Caelo	Metronidazole	12339504	6
Caelo	Metronidazole	2071304	1
Caelo	Metronidazole	20121121	1
Caelo	Metronidazole	2813E1870	1
Caelo	Metronidazole	121104085	1
Caelo	Metronidazole	12339509	4
Caelo	Metronidazole	12359501	1
Caelo	Metronidazole	1210411	1
Caelo	Metronidazole	14111304	1
Caelo	Metronidazole	8012014B	1
Caelo	Metronidazole	18051201	1
Caelo	Metronidazole	13095003	11
Caelo	Metronidazole	13095005	4
Caelo	Metronidazole	13095004	11
Caelo	Metronidazole	7031401	1
Caelo	Metronidazole	18071401	1
Caelo	Metronidazole	13095013	13
Caelo	Metronidazole	7071405	1
Caelo	Metronidazole	13095011	3
Caelo	Metronidazole	9715621	1
Caelo	Metronidazole	13214001	13
Caelo	Metronidazole	12091403	1
Caelo	Metronidazole	27092014A	1
Caelo	Metronidazole	1307002	1
Caelo	Metronidazole	13095019	7
Caelo	Metronidazole	13095017	2
Caelo	Metronidazole	13214009	7
Caelo	Metronidazole	13095018	6
Caelo	Metronidazole	23011504	1
Caelo	Metronidazole	2022015B	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Metronidazole	13214014	9
Caelo	Metronidazole	13214011	1
Caelo	Metronidazole	13214017	3
Caelo	Metronidazole	13041503	1
Caelo	Metronidazole	1321409	1
Caelo	Metronidazole	14C14-B02-291237	1
Caelo	Metronidazole	14B27-B31-291230	1
Caelo	Metronidazole	13214018	4
Caelo	Metronidazole	13214025	6
Caelo	Metronidazole	13214021	1
Caelo	Metronidazole	13214029	8
Caelo	Metronidazole	12081507	1
Caelo	Metronidazole	15215107	1
Caelo	Metronidazole	15215108	8
Caelo	Metronidazole	15215106	5
Caelo	Metronidazole	15253001	11
Caelo	Metronidazole	15253013	10
Caelo	Metronidazole	15253002	3
Caelo	Metronidazole	15253006	10
Caelo	Metronidazole	2750	1
Caelo	Metronidazole	15253011	10
Caelo	Metronidazole	15253015	10
Caelo	Metronidazole	15253016	11
Caelo	Metronidazole	1525016	1
Caelo	Metronidazole	1523017	1
Caelo	Metronidazole	16253015	1
Caelo	Metronidazole	15A20-B07-303298	1
Caelo	Metronidazole	15253021	6
Caelo	Metronidazole	15258016	1
Caelo	Metronidazole	15253022	3
Caelo	Metronidazole	15253024	11
Caelo	Metronidazole	15253026	19
Caelo	Metronidazole	15253028	9
Caelo	Metronidazole	16089201	4
Caelo	Metronidazole	16089212	16
Caelo	Metronidazole	16/19-B04-326155	1
Caelo	Metronidazole	10112903	1
Caelo	Metronidazole	23021713	1
Caelo	Metronidazole	16089225	1
Caelo	Metronidazole	1619-b04-326150	1
Caelo	Metronidazole	16/19-B04-326150	1
Caelo	Metronidazole	16089223	4
Caelo	Metronidazole	16I19-B04-329167	1
Caelo	Metronidazole	16089222	11
Caelo	Metronidazole	16089123	1
Caelo	Metronidazole	16051703	1
Caelo	Metronidazole	16089229	12
Caelo	Metronidazole	16089228	12
Caelo	Metronidazole	160892365302	1
Caelo	Metronidazole	17058001	10
Caelo	Metronidazole	7091714	1
Caelo	Metronidazole	17058005	11
Caelo	Metronidazole	1612013-01	1
Caelo	Metronidazole	17058004	5
Caelo	Metronidazole	1701039-01	2
Caelo	Metronidazole	170580035444	1
Caelo	Metronidazole	1407003-2	1
Caelo	Metronidazole	1705801	1
Caelo	Metronidazole	17058017	13
Caelo	Metronidazole	17058011	11

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Metronidazole	170580165554	1
Caelo	Metronidazole	280218010	1
Caelo	Metronidazole	1061804	2
Caelo	Metronidazole	18061803	1
Caelo	Metronidazole	17290512	14
Caelo	Metronidazole	180264001	1
Caelo	Metronidazole	19011909	1
Caelo	Metronidazole	17290525	26
Caelo	Metronidazole	1729027	1
Caelo	Metronidazole	17290526	6
Caelo	Metronidazole	19010201	3
Caelo	Metronidazole	19010210	3
Caelo	Metronidazole	19010211	6
Caelo	Metronidazole	12339510	9
Caelo	Metronidazole	15253013/2016030911	1
Caelo	Metronidazole	10112907	1
Caelo	Metronidazole	10368319	1
Caelo	Metronidazole	15253032	11
Caelo	Metronidazole	15253019	3
Caelo	Metronidazole	1307042-01	1
Caelo	Metronidazole	12339508	4
Caelo	Metronidazole	1201156	1
Caelo	Metronidazole	15215104	5
Caelo	Metronidazole	15253020	5
Caelo	Metronidazole	3947/V04/16	1
Caelo	Metronidazole	14C14-B02-291276	1
Caelo	Metronidazole	1412016-02	1
Caelo	Metronidazole	1609028-01	4
Caelo	Metronidazole	17058015	13
Caelo	Metronidazole	16089224	4
Caelo	Metronidazole	17058010	8
Caelo	Metronidazole	13214002	17
Caelo	Metronidazole	1412016-01	4
Caelo	Metronidazole	19010215	4
Caelo	Metronidazole	13214010	4
Caelo	Metronidazole	1523013	1
Caelo	Metronidazole	15215103	4
Caelo	Metronidazole	11319818	2
Caelo	Metronidazole	17290527	20
Caelo	Metronidazole	12110415	4
Caelo	Metronidazole	1307002-02	1
Caelo	Metronidazole	12110422	15
Caelo	Metronidazole	12339511	14
Caelo	Metronidazole	17058003	9
Caelo	Metronidazole	16089228-20170818Ma4	1
Caelo	Metronidazole	17058013-20180404Ma4	1
Caelo	Metronidazole	1523026	1
Caelo	Metronidazole	17058002	5
Caelo	Metronidazole	17290519	4
Caelo	Metronidazole	49(17290526)	1
Caelo	Metronidazole	17290517	24
Caelo	Metronidazole	17290507	15
Caelo	Metronidazole	121203001	2
Caelo	Metronidazole	17058016	17
Caelo	Metronidazole	14C14-B02-291239	1
Caelo	Metronidazole	19010203	11
Caelo	Metronidazole	17290504	13
Caelo	Metronidazole	16089215	13
Caelo	Metronidazole	17290503	13
Caelo	Metronidazole	3301	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Metronidazole	13214013	1
Caelo	Metronidazole	17058019	13
Caelo	Metronidazole	17290533	4
Caelo	Metronidazole	12339507	7
Caelo	Metronidazole	13095001	10
Caelo	Metronidazole	10368318	1
Caelo	Metronidazole	13214012	3
Caelo	Metronidazole	17290506	18
Caelo	Metronidazole	19010202	5
Caelo	Metronidazole	16089216	6
Caelo	Metronidazole	11319823	5
Caelo	Metronidazole	10368311	1
Caelo	Metronidazole	15253017	12
Caelo	Metronidazole	12110403	1
Caelo	Metronidazole	11319807	1
Caelo	Metronidazole	12339502	18
Caelo	Metronidazole	2013U-01870	1
Caelo	Metronidazole	1212030-21	1
Caelo	Metronidazole	132140022	1
Caelo	Metronidazole	13214024	3
Caelo	Metronidazole	14b27-b31-291230	1
Caelo	Metronidazole	14c14-b01-295545	1
Caelo	Metronidazole	17058012	14
Caelo	Metronidazole	16089231	2
Caelo	Metronidazole	18026401	9
Caelo	Metronidazole	1707008-01	3
Caelo	Metronidazole	17290518	26
Caelo	Metronidazole	1790517	1
Caelo	Metronidazole	19010213	2
Caelo	Metronidazole	1901020	1
Caelo	Metronidazole	170580001	2
Caelo	Metronidazole	17058013-20180619Ma6	1
Caelo	Metronidazole	17290509	6
Caelo	Metronidazole	15253027	10
Caelo	Metronidazole	11319810	2
Caelo	Metronidazole	1112028-01	1
Caelo	Metronidazole	13095020	5
Caelo	Metronidazole	10368310	1
Caelo	Metronidazole	12339520	4
Caelo	Metronidazole	13095002	8
Caelo	Metronidazole	13214003	11
Caelo	Metronidazole	13214015	8
Caelo	Metronidazole	15253004	13
Caelo	Metronidazole	15253005	3
Caelo	Metronidazole	15253018	5
Caelo	Metronidazole	16089221	7
Caelo	Metronidazole	16089220	15
Caelo	Metronidazole	16089235	6
Caelo	Metronidazole	16056235	1
Caelo	Metronidazole	170580123	1
Caelo	Metronidazole	17058014	13
Caelo	Metronidazole	17290515	3
Caelo	Metronidazole	19000516001	1
Caelo	Metronidazole	1807039-01	1
Caelo	Metronidazole	12110413	4
Caelo	Metronidazole	13095012	12
Caelo	Metronidazole	1523006	1
Caelo	Metronidazole	614U1870	1
Caelo	Metronidazole	13J21-N07	1
Caelo	Metronidazole	13214016	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Metronidazole	11F15-N07	1
Caelo	Metronidazole	15253007	13
Caelo	Metronidazole	15253029	5
Caelo	Metronidazole	16089202	9
Caelo	Metronidazole	19010214	7
Caelo	Metronidazole	19012011	1
Caelo	Metronidazole	19010212	3
Caelo	Metronidazole	12339526	1
Caelo	Metronidazole	15253003	8
Caelo	Metronidazole	15215105	1
Caelo	Metronidazole	160902801	1
Caelo	Metronidazole	16089213	16
Caelo	Metronidazole	16089218	9
Caelo	Metronidazole	16089217	8
Caelo	Metronidazole	16089219	8
Caelo	Metronidazole	1505024-01	1
Caelo	Metronidazole	1790512	1
Caelo	Metronidazole	17290513	4
Caelo	Metronidazole	17C10-B04-346275	1
Caelo	Metronidazole	1901210	1
Caelo	Metronidazole	113214021	1
Caelo	Metronidazole	15A20-B07-303293	1
Caelo	Metronidazole	172905125723	1
Caelo	Metronidazole	12110405	8
Caelo	Metronidazole	12339521	1
Caelo	Metronidazole	1407003-01	1
Caelo	Metronidazole	13214019	6
Caelo	Metronidazole	15A20-B07-303297	1
Caelo	Metronidazole	1505024-02	2
Caelo	Metronidazole	17058018	14
Caecolo/Phönix	Metronidazole	16089228	1
Caesar & Lorenz	Metronidazole	13095013	1
Caesar & Loretz GmbH	Metronidazole	15253017	1
Caesar & Loretz GmbH	Metronidazole	16089224	1
Caesar & Loretz GmbH	Metronidazole	17058027	1
Caesar & Loretz GmbH	Metronidazole	17290517	1
Caesar & Loretz GmbH	Metronidazole	17290526	5
Caesar & Loretz GmbH	Metronidazole	17290527	2
Caesar & Loretz GmbH	Metronidazole	19010201	3
Caesar & Loretz GmbH	Metronidazole	19010202	2
Caesar & Loretz GmbH	Metronidazole	19010203	2
Caesar & Loretz GmbH	Metronidazole	17290533	1
Caesar & Loretz GmbH	Metronidazole	19010213	3
Caesar & Loretz GmbH	Metronidazole	19010215	1
Caesar & Loretz GmbH	Metronidazole	19010211	2
Caesar & Loretz GmbH	Metronidazole	19010214	1
Caesar & Loretz GmbH	Metronidazole	19010216	2
Caesar & Loretz GmbH	Metronidazole	190102003	1
Caesar & Loretz GmbH / ...	Metronidazole	17058001	1
Caesar & Loretz GmbH / ...	Metronidazole	19010212	1
Caesar & Loretz GmbH/gehe	Metronidazole	19010202	1
Caesar & Loretz GmbH/Ge...	Metronidazole	19000516003	1
Caesar & Loretz GmbH/Go...	Metronidazole	19010214	1
Caesar&Loretz GmbH/Anzag	Metronidazole	12339511	1
Caesar&Loretz GmbH/Sana...	Metronidazole	15253003	1
Caesar&loretz,Phoenix	Metronidazole	12110410	1
Cealo/ Gehe	Metronidazole	19010213	1
Cealo/Gehe	Metronidazole	17290506	1
Cealo/Sanacorp	Metronidazole	13095003	1
Corden Pharma	Metronidazole	1212001-02	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Corden Pharma Bergamo S.p	Metronidazole	1807039-02	2
Delta	Metronidazole	17058001	1
Delta	Metronidazole	17290503	2
E Plus	Metronidazole	1707008-01	1
Ebert-Jacobi	Metronidazole	16089224	1
Euro OTC	Metronidazole	176022-01	1
eurho	Metronidazole	1612013-01	1
Eurho	Metronidazole	1406010-01	1
EuRho	Metronidazole	1109030-02	1
EuRho	Metronidazole	110903002	1
EuRho	Metronidazole	1212001-02	1
EuRho	Metronidazole	1406010-01	1
EuRho	Metronidazole	1407003-01	1
EuRho	Metronidazole	1701039-01	1
EuRho	Metronidazole	1707008-01	1
EuRho	Metronidazole	1807039-01	2
EuRho	Metronidazole	1612013-02	5
EuRho	Metronidazole	1802007-02	1
EuRho/Noweda	Metronidazole	180601M1706022-01	1
EuRho/Phönix	Metronidazole	1307002-01	1
Eurimpharm	Metronidazole	140601001	1
EURO / Sanacorp	Metronidazole	160902801	1
Euro OTC	Metronidazole	15a20-b07-303294	1
Euro OTC	Metronidazole	10800401	1
Euro OTC	Metronidazole	1112028-01	4
Euro OTC	Metronidazole	110903002	1
Euro OTC	Metronidazole	20111025	1
Euro OTC	Metronidazole	1109030-03	2
Euro OTC	Metronidazole	1307002-02	1
Euro OTC	Metronidazole	1412016-01	13
Euro OTC	Metronidazole	1407003	1
Euro OTC	Metronidazole	13070002-02	1
Euro OTC	Metronidazole	1412016	1
Euro OTC	Metronidazole	150502401	1
Euro OTC	Metronidazole	300915ME	1
Euro OTC	Metronidazole	1609023-01	1
Euro OTC	Metronidazole	1701039-01	39
Euro OTC	Metronidazole	16089224	1
Euro OTC	Metronidazole	F160028	1
Euro OTC	Metronidazole	1307002-01	11
Euro OTC	Metronidazole	1701039	2
Euro OTC	Metronidazole	F120017	1
Euro OTC	Metronidazole	1307042-02	7
Euro OTC	Metronidazole	1707088-01	2
Euro OTC	Metronidazole	1706022-02	2
Euro OTC	Metronidazole	1307042-01	9
Euro OTC	Metronidazole	1807039/01	1
Euro OTC	Metronidazole	1109030-02	1
Euro OTC	Metronidazole	1508004-02	10
Euro OTC	Metronidazole	C04-160812	1
Euro OTC	Metronidazole	150800401	1
Euro OTC	Metronidazole	121001-02	3
Euro OTC	Metronidazole	130704201	1
Euro OTC	Metronidazole	1406010-01	19
Euro OTC	Metronidazole	1407003-01	5
Euro OTC	Metronidazole	150800	1
Euro OTC	Metronidazole	1606028	1
Euro OTC	Metronidazole	1612013-02	3
Euro OTC	Metronidazole	1901042-02	1
Euro OTC	Metronidazole	1109030-01	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Metronidazole	1112028-02	7
Euro OTC	Metronidazole	700837	1
Euro OTC	Metronidazole	140601001	2
Euro OTC	Metronidazole	1802007-02	3
Euro OTC	Metronidazole	1901042-01	3
Euro OTC	Metronidazole	1807039-03	6
Euro OTC	Metronidazole	1906012-01	1
Euro OTC	Metronidazole	1212001-01	8
Euro OTC	Metronidazole	170700801	2
Euro OTC	Metronidazole	1412016-02	20
Euro OTC	Metronidazole	1308704201	1
Euro OTC	Metronidazole	150502402	1
Euro OTC	Metronidazole	1703028-01	1
Euro OTC	Metronidazole	1707008-01	33
Euro OTC	Metronidazole	1609028-02	9
Euro OTC	Metronidazole	1407003-02	8
Euro OTC	Metronidazole	1212030-01	3
Euro OTC	Metronidazole	1212001-02	13
Euro OTC	Metronidazole	140700301	1
Euro OTC	Metronidazole	140700302	2
Euro OTC	Metronidazole	1505024-02	6
Euro OTC	Metronidazole	1609028	2
Euro OTC	Metronidazole	1612013-01	18
Euro OTC	Metronidazole	17290513	1
Euro OTC	Metronidazole	1707039-01	1
Euro OTC	Metronidazole	161201301	1
Euro OTC	Metronidazole	13B06-N03	1
Euro OTC	Metronidazole	169028-01	1
Euro OTC	Metronidazole	190104201	1
Euro/ Sanacorp	Metronidazole	150800402	1
Euro/Noweda	Metronidazole	1609028-01	1
Euro OTC	Metronidazole	13214010	1
Euro/Sanacorp	Metronidazole	1609028	1
Euro OTC	Metronidazole	1508004-01	24
Euro OTC	Metronidazole	1503004-01	1
Euro OTC	Metronidazole	1807039-01	15
Euro OTC	Metronidazole	1505024-01	11
Euro OTC	Metronidazole	1706022-01	11
Euro OTC	Metronidazole	1802007-01	7
Euro OTC	Metronidazole	17058005	1
Euro OTC	Metronidazole	1908028-01	1
Euro OTC	Metronidazole	170700802	1
Euro OTC	Metronidazole	1505024-03	3
EuroPharma	Metronidazole	141201601	1
Fagron	Metronidazole	14C14-B01-295548	1
Fagron	Metronidazole	12L17_N16	1
Fagron	Metronidazole	14C14B02	3
Fagron	Metronidazole	16/19-B04-326154	1
Fagron	Metronidazole	12F15-N04	7
Fagron	Metronidazole	11F15-N07	1
Fagron	Metronidazole	12a2o-n18	1
Fagron	Metronidazole	12D30-N03	4
Fagron	Metronidazole	12L17N11	1
Fagron	Metronidazole	3212E01870	1
Fagron	Metronidazole	12L17-N16	6
Fagron	Metronidazole	11J07-N07	1
Fagron	Metronidazole	9041303	1
Fagron	Metronidazole	12L-N11	1
Fagron	Metronidazole	13D08N22	1
Fagron	Metronidazole	13D08-N22	6

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Metronidazole	13B06N03	1
Fagron	Metronidazole	20121121	3
Fagron	Metronidazole	11C21-N01	1
Fagron	Metronidazole	13J21-N07	35
Fagron	Metronidazole	13J21N07	2
Fagron	Metronidazole	13/10-No3	1
Fagron	Metronidazole	13I10-N03	3
Fagron	Metronidazole	1414-B02-291237	1
Fagron	Metronidazole	13095002	1
Fagron	Metronidazole	13j21-n07	2
Fagron	Metronidazole	14C14-B02-291237	8
Fagron	Metronidazole	14B27-B31-291234	1
Fagron	Metronidazole	13j21-N07	1
Fagron	Metronidazole	14C14-B02	4
Fagron	Metronidazole	14c14b02291276	1
Fagron	Metronidazole	14C14-B02-291275	4
Fagron	Metronidazole	12f15-n04	1
Fagron	Metronidazole	20140131F	3
Fagron	Metronidazole	14c14-b02-291276	2
Fagron	Metronidazole	14C14-B02-291238	2
Fagron	Metronidazole	14c14-b02-291239	1
Fagron	Metronidazole	14C14-Bo2-291276	1
Fagron	Metronidazole	14C14B02-291276	2
Fagron	Metronidazole	14c14-b02-291275	1
Fagron	Metronidazole	14C14-B291237	1
Fagron	Metronidazole	14C14-B02_291238	1
Fagron	Metronidazole	14C14-B02-296437	10
Fagron	Metronidazole	14C14-B02-300182	3
Fagron	Metronidazole	1220141155F	2
Fagron	Metronidazole	15A20-B07-303294	3
Fagron	Metronidazole	15A20-B07-303295	1
Fagron	Metronidazole	14-C14-B02-296437	1
Fagron	Metronidazole	140700301	1
Fagron	Metronidazole	15A20-B07-308196	3
Fagron	Metronidazole	15A20-B07-308525	6
Fagron	Metronidazole	15A20-B07	1
Fagron	Metronidazole	15a20-b07-308196	1
Fagron	Metronidazole	15a20-b07-308791	1
Fagron	Metronidazole	15A20Bo7308196	1
Fagron	Metronidazole	15A20-B07-303298	8
Fagron	Metronidazole	12A20-B07-303298	1
Fagron	Metronidazole	15A20-B07-312057	4
Fagron	Metronidazole	15A20-B07312057	1
Fagron	Metronidazole	15a20b07303298	1
Fagron	Metronidazole	15A20-B07-31225	1
Fagron	Metronidazole	15253017	2
Fagron	Metronidazole	16D15-B50-324137	2
Fagron	Metronidazole	19119-B04-326154	1
Fagron	Metronidazole	16/19-B04-326155	2
Fagron	Metronidazole	16I19-B04-326151	4
Fagron	Metronidazole	16/19bo4326155	1
Fagron	Metronidazole	1619-B04-326155	1
Fagron	Metronidazole	16I19-B04-326152	2
Fagron	Metronidazole	16I19-B04-329167	2
Fagron	Metronidazole	160902	1
Fagron	Metronidazole	16/19-B04	2
Fagron	Metronidazole	1619b04326155	1
Fagron	Metronidazole	16/19-B04-326152	1
Fagron	Metronidazole	17/19-304-329168	1
Fagron	Metronidazole	16/19-B04-329168	3

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Metronidazole	606/10072017	1
Fagron	Metronidazole	1619B04329161	1
Fagron	Metronidazole	16/19-b04-329168	1
Fagron	Metronidazole	17058003	1
Fagron	Metronidazole	16I19-B04-329165	1
Fagron	Metronidazole	1612013-01	3
Fagron	Metronidazole	15A20-B07-308198	1
Fagron	Metronidazole	16I19-B04-329162	1
Fagron	Metronidazole	16/19-B04-329160	1
Fagron	Metronidazole	17C10-B04-338707	1
Fagron	Metronidazole	16/19-B04-329163	1
Fagron	Metronidazole	17C10	1
Fagron	Metronidazole	17C10-B04	3
Fagron	Metronidazole	17C10-B04-346279	1
Fagron	Metronidazole	17C10-B04-346277	2
Fagron	Metronidazole	17c10-b04-346276	1
Fagron	Metronidazole	18B28-B50-354849	1
Fagron	Metronidazole	61021826	1
Fagron	Metronidazole	20140131f	1
Fagron	Metronidazole	601021826	1
Fagron	Metronidazole	112356	1
Fagron	Metronidazole	14C14-B02-291239	6
Fagron	Metronidazole	14c14-B01-295545	1
Fagron	Metronidazole	12D30-N02	1
Fagron	Metronidazole	172939-B01-295547	1
Fagron	Metronidazole	16/19-B04-329167	2
Fagron	Metronidazole	605021726	3
Fagron	Metronidazole	16I19-B04	3
Fagron	Metronidazole	18B28-B50-354847	1
Fagron	Metronidazole	17C10-B04-355863	1
Fagron	Metronidazole	48(17C10-B04-346277	1
Fagron	Metronidazole	1412016-01	1
Fagron	Metronidazole	17C10-B04-346276	8
Fagron	Metronidazole	15A20-B07-303294Mg	1
Fagron	Metronidazole	19G02-B04-362816	1
Fagron	Metronidazole	14C14-B02-291276	3
Fagron	Metronidazole	13B06-N03	10
Fagron	Metronidazole	14C14-B02-291241	1
Fagron	Metronidazole	19G02-B04-362813	1
Fagron	Metronidazole	1802007-01	1
Fagron	Metronidazole	15A20-B07-308791	3
Fagron	Metronidazole	1609028-01	2
Fagron	Metronidazole	14C14-B01-309058	2
Fagron	Metronidazole	16/19-B04-326151	2
Fagron	Metronidazole	15A20/B07-303298	1
Fagron	Metronidazole	15A20-B07-303293	9
Fagron	Metronidazole	15A20-B07-312225	3
Fagron	Metronidazole	16/16-B04-326151	1
Fagron	Metronidazole	16I19-B04-329159	1
Fagron	Metronidazole	17058013	1
Fagron	Metronidazole	12d30-n03	1
Fagron	Metronidazole	16J19-B04-326151	1
Fagron	Metronidazole	14C14-B01-306363	5
Fagron	Metronidazole	14C14-B02-295603	1
Fagron	Metronidazole	14C14-B01-295548	1
Fagron	Metronidazole	16/19-B04-326150	6
Fagron	Metronidazole	16I19-B04-326150	1
Fagron	Metronidazole	604081626	2
Fagron	Metronidazole	16I19-B04-329160	2
Fagron	Metronidazole	17C10-B04-346275	3

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Metronidazole	20130906F	4
Fagron	Metronidazole	14C14-802-291237	1
Fagron	Metronidazole	10F23-N05	1
Fagron	Metronidazole	13/21-N07	1
Fagron	Metronidazole	14C14-B02-2911239	1
Fagron	Metronidazole	16I19-B04-326150	3
Fagron	Metronidazole	17C10-B04-355865	2
Fagron	Metronidazole	12L17-N11	15
Fagron	Metronidazole	PM41	1
Fagron	Metronidazole	14B27-B31-291235	1
Fagron	Metronidazole	14C14-B01	1
Fagron	Metronidazole	141C14-B02-296437	1
Fagron	Metronidazole	15A20B07308525	1
Fagron	Metronidazole	1508004-01	1
Fagron	Metronidazole	1619-B04-326150	1
Fagron	Metronidazole	16I19-B04-329161	1
Fagron	Metronidazole	17C10-B04-346280	1
Fagron	Metronidazole	1802007-02	1
Fagron	Metronidazole	12117-n11	1
Farchemia S. r. l.	Metronidazole	1609028-01	1
Farchemia S.R.L./ Caesa...	Metronidazole	15253032	1
Farchemia/Phönix	Metronidazole	1609028-02	1
Fargon	Metronidazole	13D08-N22	1
Fargon	Metronidazole	14c14-b02-291238	1
Fiebig	Metronidazole	16089235	1
Fiebig	Metronidazole	17058005	1
Fiebig	Metronidazole	17058027	1
Fiebig	Metronidazole	17290506	1
Fiebig	Metronidazole	17290507	1
Fiebig	Metronidazole	17290504	1
Fiebig	Metronidazole	17290517	2
Fiebig	Metronidazole	17290527	1
Fiebig	Metronidazole	17290532	1
Fischer/Gehe	Metronidazole	15A20-B07-308525	1
Frago/Noweda	Metronidazole	16I19-B04-329163	1
Gatt-Koller	Metronidazole	497/03151015	1
Gatt-Koller	Metronidazole	606293914	1
Gatt-Koller	Metronidazole	497/03151515	1
Gatt-Koller	Metronidazole	497/03154015	1
Gatt-Koller	Metronidazole	3728/11162017	1
Gehe	Metronidazole	10368318	1
Gehe	Metronidazole	12110422	1
Gehe	Metronidazole	12110415	1
Gehe	Metronidazole	1112028-02	1
Gehe	Metronidazole	1307002-01	1
Gehe	Metronidazole	1307002-02	1
Gehe	Metronidazole	1407003-01	2
Gehe	Metronidazole	1505024-01	1
Gehe	Metronidazole	16H15-B50-326734	1
Gehe	Metronidazole	15253026	1
Gehe	Metronidazole	17058016	1
Gehe	Metronidazole	17290506	1
GEHE	Metronidazole	15253032	1
GEHE	Metronidazole	16089216	1
GEHE	Metronidazole	16089229	1
GEHE	Metronidazole	17058013	1
GEHE	Metronidazole	17058015	1
GEHE 11.06.2014	Metronidazole	1307002-01	1
Gehe 23.11.18	Metronidazole	1706022-02	1
Gehe am 04.02.14	Metronidazole	1212030-01	2

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Metronidazole	16089215/1140217	1
Caelo	Metronidazole	17058027	7
Euro OTC	Metronidazole	1807039	1
Gehe01/2018	Metronidazole	14C14-B02-291237	1
GH: ...	Metronidazole	17290503	1
Henry Lamotte	Metronidazole	1212001-02	1
Hubei Hongyuan	Metronidazole	140700301	1
Ichthyol Gesellschaft	Metronidazole	13095005	1
Ichthyol/ALH	Metronidazole	1609028-02	1
Infectopharm / Alliance	Metronidazole	18B28-B50-354849	1
Caelo	Metronidazole	1790504	1
Kehr	Metronidazole	17058003	1
Kehr	Metronidazole	17290512	1
Klosterring	Metronidazole	16089235	1
krieger	Metronidazole	19010203	1
Kuerzel	Metronidazole	1307002-02	1
L10	Metronidazole	1807039-01	4
L12	Metronidazole	1609028-02	1
L12	Metronidazole	1609028-01	1
L30	Metronidazole	16089224	2
Noweda	Metronidazole	11319818	1
Noweda	Metronidazole	12110404	1
Noweda	Metronidazole	12G04-N15	1
Noweda	Metronidazole	12339501	1
Noweda	Metronidazole	13095012	1
Noweda	Metronidazole	1407003-01	2
Noweda	Metronidazole	13214025	1
Noweda	Metronidazole	1505024-03	1
Noweda	Metronidazole	160902802	1
Noweda	Metronidazole	17058005	2
Noweda	Metronidazole	1619-B04-329166	1
Noweda	Metronidazole	17058013	1
Noweda	Metronidazole	1701039-01	1
Noweda	Metronidazole	17058014	1
Noweda	Metronidazole	17290518	1
Caelo	Metronidazole	1508004-02	1
Caelo	Metronidazole	161201301	1
Caelo	Metronidazole	12110412	5
Caelo	Metronidazole	13095006	6
Noweda 27.11.2019	Metronidazole	19010211	1
Fagron	Metronidazole	16L19_B04_326152	1
Caelo	Metronidazole	15253033	6
Caelo	Metronidazole	16089236	2
Caelo	Metronidazole	16/19-B04-329160	1
Euro OTC	Metronidazole	150804-01	1
Noweda/Wepa	Metronidazole	13214017	1
Euro OTC	Metronidazole	14120601	1
Caelo	Metronidazole	17290532	8
Phoenix	Metronidazole	121203002	1
Phoenix	Metronidazole	16089201	1
Phoenix	Metronidazole	15253032	1
Phoenix	Metronidazole	16089224	1
Phoenix	Metronidazole	17058002	1
Phoenix	Metronidazole	17058027	1
Phoenix	Metronidazole	17058026	1
Phoenix	Metronidazole	17290527	2
Phoenix	Metronidazole	19010202	1
Phoenix	Metronidazole	17290517	1
Phoenix	Metronidazole	3403	1
Phoenix 11.09.13	Metronidazole	12L17-N11	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Phoenix 12.10.2016 6,63EUR	Metronidazole	15253027	1
Phoenix 4.3.2019	Metronidazole	17290526	1
Caelo	Metronidazole	17058012/2231117	1
Fagron	Metronidazole	16H15-B50-326734	1
Phoenix/Cealo	Metronidazole	17058016/0818E-0187	1
Phonix	Metronidazole	1612013-01	1
phönix	Metronidazole	15253026	1
Phönix	Metronidazole	1109030-03	1
Phönix	Metronidazole	12L17-N11	1
Phönix	Metronidazole	121203001	1
Phönix	Metronidazole	13J21-N07	1
Phönix	Metronidazole	13214017	2
Phönix	Metronidazole	15253018	1
Phönix	Metronidazole	16089212	1
Phönix	Metronidazole	1701039-01	1
Phönix	Metronidazole	17058016	1
Phönix	Metronidazole	17058003	1
Phönix	Metronidazole	3179	1
Phönix	Metronidazole	1807039-01	1
Phönix	Metronidazole	19010210	1
PHÖNIX	Metronidazole	17058011	3
Euro OTC	Metronidazole	1609028-01	26
Phönix Gotha	Metronidazole	13214017	1
Euro OTC	Metronidazole	170103901	1
Caelo	Metronidazole	1508004-01	1
Caelo	Metronidazole	17058013	13
Caelo	Metronidazole	1706022-01	2
Euro OTC	Metronidazole	1807039-02	11
Phönix_ 13.12.2018	Metronidazole	17290518	1
Reichelt	Metronidazole	17058013	1
Sana	Metronidazole	19010210	1
Sanacorp	Metronidazole	12110422	1
Sanacorp	Metronidazole	12G04-N15	1
Sanacorp	Metronidazole	12339519	1
Sanacorp	Metronidazole	39AKD15	1
Sanacorp	Metronidazole	13095002	1
Sanacorp	Metronidazole	39/AKD18	1
Sanacorp	Metronidazole	39/AKD6	1
Sanacorp	Metronidazole	16I19-B04-329159	1
Sanacorp	Metronidazole	17058002	1
Sanacorp	Metronidazole	16I19-B04-329160	1
Sanacorp	Metronidazole	1707008-01	1
Sanacorp	Metronidazole	1701039-01	1
Sanacorp	Metronidazole	17058018	1
Sanacorp	Metronidazole	17C10-B04-338707	1
Sanacorp	Metronidazole	17C10-B04-346280	2
Sanacorp	Metronidazole	17290512	1
Sanacorp	Metronidazole	601021826	1
Sanacorp	Metronidazole	17290518	1
Sanacorp	Metronidazole	17290533	1
Sanacorp 27.10.15	Metronidazole	15A20-B07-303298	1
Sanacorp 02.03.15	Metronidazole	13214009	1
Caelo	Metronidazole	11h11-n03	1
Caelo	Metronidazole	11319816	2
Euro OTC	Metronidazole	1109016-01	1
Fagron	Metronidazole	12G04-N15	15
Caelo	Metronidazole	39/AKD16	1
Caelo	Metronidazole	39/AKD4	1
Caelo	Metronidazole	16089209	14
Euro OTC	Metronidazole	1707008-02	4

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continued from previous page

Supplier	Substance	Batch	Spectra
Spangro 28.05.2014	Metronidazole	13/10-N03	1
Spangropharm	Metronidazole	11319818	1
vdl	Metronidazole	12110421	1
WE Alliance Healthcare ...	Metronidazole	19010201	1
WEPA/Gehe	Metronidazole	20180515-04P	1
ACM	Metronidazole		1
Caelo	Metronidazole	13095007	5
Caelo	Metronidazole		5
Euro OTC	Metronidazole	1212030-02	7
Euro OTC	Metronidazole		2
Euro OTC	Metronidazole	1508004	1
Fagron	Metronidazole	13D10-N02	4
Fagron	Metronidazole		1
Fagron	Metronidazole	16I19-B04-326155	3
	Metronidazole	15253007	2
Phoenix	Metronidazole		1
Sanacorp	Metronidazole		1

- 108 779 spectra from 742 *Apo-Ident* customers from a total of 31 376 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Metronidazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Metronidazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	540	0	118 602
Type C	0	2450	18	108 779

The substance/substance group *Metronidazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8889 %)
Type C	100.0000 % (> 99.8899 %)	99.2707 % (> 99.1491 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Metronidazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	70.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Metronidazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21212	21881	3.15	71.89
21213	21881	2.95	71.24
21356	21881	3.77	72.33
21360	21881	3.02	71.59
21881	21881	0.00	71.44
22472	22472	0.00	71.84
22835	22472	1.90	72.44
20857	21881	5.60	73.54

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Miconazole nitrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20210-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Miconazole nitrate; Miconazoli nitras

Special notes

When selecting the *Miconazole nitrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Miconazole nitrate	7	11	288

Second-stage model

For differentiation of the substance/substance group *Miconazole nitrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Miconazole nitrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Miconazole nitrate	13185601	20875	40	20130704
Caelo	Miconazole nitrate	13185601	20905	80	20130704
Caelo	Miconazole nitrate	13352802	21350	39	1412250
Caelo	Miconazole nitrate	13352802	21351	40	20131118
Caelo	Miconazole nitrate	161447	22630	40	20160617*
Euro OTC	Miconazole nitrate	1307025-02	21649	60	20130806
Euro OTC	Miconazole nitrate	1509014	21900	60	20150930*
Fagron	Miconazole nitrate	13D22-N14	20817	100	20130529
Fagron	Miconazole nitrate	18C23-B02-356141	24593	40	20180416

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 499 spectra of 9 reference samples from the substance/substance group *Miconazole nitrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 190 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 723 spectra of 18 reference samples from the substance/substance group *Miconazole nitrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Miconazole nitrate	172175	23662	30
Caelo	Miconazole nitrate	182821	24388	40
Euro OTC	Miconazole nitrate	1604004	22522	40
Euro OTC	Miconazole nitrate	1607004	22671	40
Euro OTC	Miconazole nitrate	1611024	22920	40
Euro OTC	Miconazole nitrate	1705039	23429	40
Euro OTC	Miconazole nitrate	1710020	23775	40
Euro OTC	Miconazole nitrate	1803028	24071	40
Euro OTC	Miconazole nitrate	1811015	24338	40
Euro OTC	Miconazole nitrate	1904032	24601	40
Euro OTC	Miconazole nitrate	1909029	24938	40
Caelo	Miconazole nitrate	13185601	20875SI [†]	60
Caelo	Miconazole nitrate	161447	22630SI [†]	40
Euro OTC	Miconazole nitrate	1307025-02	21649SI [†]	37
Euro OTC	Miconazole nitrate	1509014	21900SI [†]	53
Euro OTC	Miconazole nitrate	1604004	22522SI	36
Euro OTC	Miconazole nitrate	1607004	22671SI	30
Euro OTC	Miconazole nitrate	1611024	22920SI	37

- 118419 spectra from a total of 2405 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1432 spectra from 380 *Apo-Ident* customers from 316 batches from the substance/substance group *Miconazole nitrate*.
- Among them are spectra of independent samples from 288 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
20; 04.12.13	Miconazole nitrate	13185611	2
Bombastus	Miconazole nitrate	16144725	1
AHD	Miconazole nitrate	12374307	1
Fagron	Miconazole nitrate	15108-B07-318485	1
Alliance H.	Miconazole nitrate	5137910	1
Alliance Health 05.02.2...	Miconazole nitrate	13352801	2
Alliance Healthcare	Miconazole nitrate	12374307	1
Alliance Healthcare	Miconazole nitrate	1811015-01	2
Alliance Healthcare	Miconazole nitrate	18C23-B02-355295	1
Alliance Healthcare	Miconazole nitrate	18C23-B02-353243	1
Anzag	Miconazole nitrate	12243802	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Anzag	Miconazole nitrate	12374301	3
Anzag	Miconazole nitrate	15A13-B07-308432	1
Anzag	Miconazole nitrate	15137902	1
Anzag	Miconazole nitrate	16144716	1
Anzag	Miconazole nitrate	18C23-B02-353243	1
Bionorica /Phönix	Miconazole nitrate	12C13B03-279593	1
Bomastus / Alliance Hea...	Miconazole nitrate	16E04-B03-327367	1
Bombastus	Miconazole nitrate	15I08-B07-318687	1
Bombastus	Miconazole nitrate	13352806	1
Caelo	Miconazole nitrate	15108-B07-315492	1
Caelo	Miconazole nitrate	18B06_b03_34778	1
Caelo	Miconazole nitrate	11104113	1
Caelo	Miconazole nitrate	11324902	1
Caelo	Miconazole nitrate	11104109	2
Caelo	Miconazole nitrate	11104114	1
Caelo	Miconazole nitrate	11104103	2
Caelo	Miconazole nitrate	11324905	4
Caelo	Miconazole nitrate	11324912	2
Caelo	Miconazole nitrate	12243801	3
Caelo	Miconazole nitrate	11324909	1
Caelo	Miconazole nitrate	11243803	1
Caelo	Miconazole nitrate	9177904	1
Caelo	Miconazole nitrate	12k02n06	1
Caelo	Miconazole nitrate	11324913	1
Caelo	Miconazole nitrate	12243805	6
Caelo	Miconazole nitrate	11104108	1
Caelo	Miconazole nitrate	12243806	1
Caelo	Miconazole nitrate	12243808	9
Caelo	Miconazole nitrate	12374301	4
Caelo	Miconazole nitrate	12374307	15
Caelo	Miconazole nitrate	28051306	1
Caelo	Miconazole nitrate	12374308	6
Caelo	Miconazole nitrate	4061304	1
Caelo	Miconazole nitrate	13185611	15
Caelo	Miconazole nitrate	13H28-N06	1
Caelo	Miconazole nitrate	13185610	6
Caelo	Miconazole nitrate	411092-2-P	1
Caelo	Miconazole nitrate	13352805	1
Caelo	Miconazole nitrate	13342801	1
Caelo	Miconazole nitrate	14149305	1
Caelo	Miconazole nitrate	1419301	1
Caelo	Miconazole nitrate	14149301	14
Caelo	Miconazole nitrate	1307025-02	1
Caelo	Miconazole nitrate	1122014A	1
Caelo	Miconazole nitrate	14149310	8
Caelo	Miconazole nitrate	14149308	11
Caelo	Miconazole nitrate	1419310	1
Caelo	Miconazole nitrate	14149317	9
Caelo	Miconazole nitrate	15137902	19
Caelo	Miconazole nitrate	15137906	1
Caelo	Miconazole nitrate	8716	1
Caelo	Miconazole nitrate	15137903	18
Caelo	Miconazole nitrate	15137911	1
Caelo	Miconazole nitrate	15I08-B07-312317	3
Caelo	Miconazole nitrate	2747	1
Caelo	Miconazole nitrate	151379	1
Caelo	Miconazole nitrate	15137905	11
Caelo	Miconazole nitrate	2773	1
Caelo	Miconazole nitrate	2777	1
Caelo	Miconazole nitrate	2787	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Miconazole nitrate	15137908	7
Caelo	Miconazole nitrate	2796	1
Caelo	Miconazole nitrate	15137910	6
Caelo	Miconazole nitrate	15137914	5
Caelo	Miconazole nitrate	15137915	3
Caelo	Miconazole nitrate	15I08-B07-318687	2
Caelo	Miconazole nitrate	16144701	29
Caelo	Miconazole nitrate	16144704	14
Caelo	Miconazole nitrate	16144717	8
Caelo	Miconazole nitrate	16e04b03327367	1
Caelo	Miconazole nitrate	16E04-B03-325448	1
Caelo	Miconazole nitrate	16144726	12
Caelo	Miconazole nitrate	17217507	1
Caelo	Miconazole nitrate	18057904	1
Caelo	Miconazole nitrate	1727503	1
Caelo	Miconazole nitrate	18057901	1
Caelo	Miconazole nitrate	18057909	1
Caelo	Miconazole nitrate	18057916	1
Caelo	Miconazole nitrate	18057907	9
Caelo	Miconazole nitrate	18057913	12
Caelo	Miconazole nitrate	180057913	1
Caelo	Miconazole nitrate	18282105	12
Caelo	Miconazole nitrate	18C23-B02-352488	1
Caelo	Miconazole nitrate	18282109	9
Caelo	Miconazole nitrate	18282110	4
Caelo	Miconazole nitrate	14149302	15
Caelo	Miconazole nitrate	14149303	5
Caelo	Miconazole nitrate	14149309	8
Caelo	Miconazole nitrate	13185609	9
Caelo	Miconazole nitrate	14D25-B06-294959	1
Caelo	Miconazole nitrate	14H06-B01-299799	1
Caelo	Miconazole nitrate	1705039-01	1
Caelo	Miconazole nitrate	16144703	17
Caelo	Miconazole nitrate	1803028-01	1
Caelo	Miconazole nitrate	17C01B02340778	1
Caelo	Miconazole nitrate	13185602	6
Caelo	Miconazole nitrate	18282113	1
Caelo	Miconazole nitrate	15137913	4
Caelo	Miconazole nitrate	18057906	19
Caelo	Miconazole nitrate	12243802	4
Caelo	Miconazole nitrate	13D22-N14	1
Caelo	Miconazole nitrate	13185603	10
Caelo	Miconazole nitrate	18057912	9
Caelo	Miconazole nitrate	18057914	6
Caelo	Miconazole nitrate	18282106	4
Caelo	Miconazole nitrate	14B18-B02-291233	1
Caelo	Miconazole nitrate	18057903	19
Caelo	Miconazole nitrate	15137907	10
Caelo	Miconazole nitrate	16E04-B03-322124	1
Caelo	Miconazole nitrate	13352811	5
Caelo	Miconazole nitrate	14149311	14
Caelo	Miconazole nitrate	14149318	20
Caelo	Miconazole nitrate	15108-B07-314838	1
Caelo	Miconazole nitrate	15108-B07-318686	1
Caelo	Miconazole nitrate	17217502	31
Caelo	Miconazole nitrate	19A31-B01-360614	2
Caelo	Miconazole nitrate	14D25-B06-294960	3
Caelo	Miconazole nitrate	16144720	6
Caelo	Miconazole nitrate	16144721	12
Caelo	Miconazole nitrate	16144725	22

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Miconazole nitrate	11324901	1
Caelo	Miconazole nitrate	13352801	17
Caelo	Miconazole nitrate	15137909	9
Caelo	Miconazole nitrate	17217503	14
Caelo	Miconazole nitrate	16E04-B03-321367	1
Caelo	Miconazole nitrate	18057911	1
Caelo	Miconazole nitrate	18282101	1
Caelo	Miconazole nitrate	15/05-B07-312317	1
Caelo	Miconazole nitrate	15A13-B07	1
Caelo	Miconazole nitrate	16144702	22
Caelo	Miconazole nitrate	16144710	15
Caelo	Miconazole nitrate	16144716	24
Caelo	Miconazole nitrate	16144711	10
Caelo	Miconazole nitrate	15I08-B07-315481	1
Caelo	Miconazole nitrate	15/08-B07-315481	1
Caelo	Miconazole nitrate	13185612	5
Caelo	Miconazole nitrate	122438	1
Caelo	Miconazole nitrate	18057902	10
Caesar & Loretz GmbH	Miconazole nitrate	16144702	1
Caesar & Loretz GmbH	Miconazole nitrate	16144717	1
Caesar & Loretz GmbH	Miconazole nitrate	18057912	1
Caesar & Loretz GmbH	Miconazole nitrate	18057913	3
Caesar & Loretz GmbH	Miconazole nitrate	18282105	2
Caesar & Loretz GmbH	Miconazole nitrate	18282106	1
Caesar & Loretz GmbH / ...	Miconazole nitrate	18282111	1
Caesar & Loretz GmbH Hi...	Miconazole nitrate	14149301	1
Caesar & Loretz GmbH, 4...	Miconazole nitrate	11324904	1
Caesar & Loretz GmbH, 4...	Miconazole nitrate	13185602	1
Caesar & Loretz GmbH, P...	Miconazole nitrate	18282111	2
Caesar & Loretz GmbH, P...	Miconazole nitrate	18057914	1
Caesar & Loretz GmbH, P...	Miconazole nitrate	18282106	2
Caesar & Loretz GmbH/Fi...	Miconazole nitrate	18057906	1
Caesar & Loretz/AHC	Miconazole nitrate	15137910	1
Caesar und Loretz	Miconazole nitrate	12243805	1
Caesar&Loretz GmbH D-4...	Miconazole nitrate	12243808	1
Caesar&Loretz GmbH /Anzag	Miconazole nitrate	14149310	1
Caesar&Loretz GmbH/Anzag	Miconazole nitrate	13185603	1
Caesar&Loretz GmbH/Anzag	Miconazole nitrate	13352802	1
Caesar&lorenz,Phoenix	Miconazole nitrate	12374301	1
Dr. Wolff	Miconazole nitrate	18E04-B03	1
E+J, 27.09.2016	Miconazole nitrate	15137915	1
euro AHD	Miconazole nitrate	1710020-015633	1
euro AHD	Miconazole nitrate	1710020-015639	1
Euro OTC	Miconazole nitrate	1307025-01	2
Euro OTC	Miconazole nitrate	140902301	1
Euro OTC	Miconazole nitrate	140902302	1
Euro OTC	Miconazole nitrate	1604004-01	5
Euro OTC	Miconazole nitrate	1607004-01	7
Euro OTC	Miconazole nitrate	1611024-015307	1
Euro OTC	Miconazole nitrate	1611024-015330	1
Euro OTC	Miconazole nitrate	1705039-015371	1
Euro OTC	Miconazole nitrate	1705039-015432	1
Euro OTC	Miconazole nitrate	1710020-01	9
Euro OTC	Miconazole nitrate	17C01-B02-339699	1
Euro OTC	Miconazole nitrate	1710020-015457	1
Euro OTC	Miconazole nitrate	17C01-B02-341814	1
Euro OTC	Miconazole nitrate	20180430/5	1
Euro OTC	Miconazole nitrate	181101501	1
Euro OTC	Miconazole nitrate	1950000070	1
Euro OTC	Miconazole nitrate	16E04-B03-327362	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Miconazole nitrate	1409023-02	4
Euro OTC	Miconazole nitrate	1504003-01	2
Euro OTC	Miconazole nitrate	1504903-01	1
Euro OTC	Miconazole nitrate	18057907	1
Euro OTC	Miconazole nitrate	1611024-02	2
Euro OTC	Miconazole nitrate	1705039-02	6
Euro OTC	Miconazole nitrate	1803028-01	13
Euro OTC	Miconazole nitrate	1811015-01	6
Euro OTC	Miconazole nitrate	19A31-B01-359397	1
Euro OTC	Miconazole nitrate	1611024-01	7
Euro OTC	Miconazole nitrate	16E04-B03-322124	1
Euro OTC	Miconazole nitrate	1705039-01	10
Euro OTC	Miconazole nitrate	1909029-01	1
Euro/Phönix	Miconazole nitrate	1803028-01	3
Euro OTC	Miconazole nitrate	1509014-01	6
EuroPTC/Phönix	Miconazole nitrate	14149316	1
Fagron	Miconazole nitrate	1508-B07-314838	1
Fagron	Miconazole nitrate	17C01-B02-341395	4
Fagron	Miconazole nitrate	27061202	1
Fagron	Miconazole nitrate	20081201	1
Fagron	Miconazole nitrate	12A16-N02	2
Fagron	Miconazole nitrate	12H10-N02	4
Fagron	Miconazole nitrate	12/21-M03	1
Fagron	Miconazole nitrate	12K02-N06	7
Fagron	Miconazole nitrate	17011307	1
Fagron	Miconazole nitrate	2900/08/12	2
Fagron	Miconazole nitrate	13E13-N08	2
Fagron	Miconazole nitrate	13E13-N04	2
Fagron	Miconazole nitrate	13H28-N06	2
Fagron	Miconazole nitrate	13H28-N06	13
Fagron	Miconazole nitrate	31101306	1
Fagron	Miconazole nitrate	4111301	1
Fagron	Miconazole nitrate	13A14-B09	2
Fagron	Miconazole nitrate	13A14-B09-287487	3
Fagron	Miconazole nitrate	13H28_N06	1
Fagron	Miconazole nitrate	14051403	1
Fagron	Miconazole nitrate	19051402	1
Fagron	Miconazole nitrate	2900/15/13	2
Fagron	Miconazole nitrate	14B18B02	1
Fagron	Miconazole nitrate	14D25-B06-294959	8
Fagron	Miconazole nitrate	14d25-b06-294960	1
Fagron	Miconazole nitrate	14149313	1
Fagron	Miconazole nitrate	14b18-b02-291247	1
Fagron	Miconazole nitrate	14D25-B06-294960	1
Fagron	Miconazole nitrate	13061501	1
Fagron	Miconazole nitrate	15A13-B07	7
Fagron	Miconazole nitrate	14H06-B01-299799	8
Fagron	Miconazole nitrate	15A13-B07-306791	10
Fagron	Miconazole nitrate	15A13-B07-306791nron	1
Fagron	Miconazole nitrate	14b18-B02-291231	1
Fagron	Miconazole nitrate	15I08-B07	3
Fagron	Miconazole nitrate	15I08-B07-312321	8
Fagron	Miconazole nitrate	14d25-b06-299790	1
Fagron	Miconazole nitrate	2900/10/14	1
Fagron	Miconazole nitrate	14H06-B01-299798	1
Fagron	Miconazole nitrate	14H16-B01-299798	1
Fagron	Miconazole nitrate	15a13-b07-308432	1
Fagron	Miconazole nitrate	15I08-B07-3121321	1
Fagron	Miconazole nitrate	15i08-b07-312317	1
Fagron	Miconazole nitrate	2900/11/15	2

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Miconazole nitrate	15108-B07-315492	3
Fagron	Miconazole nitrate	15A13-B07-306565	1
Fagron	Miconazole nitrate	16E04-B03-321367	2
Fagron	Miconazole nitrate	15/08-B07-318686	2
Fagron	Miconazole nitrate	15i08-b07-315481	1
Fagron	Miconazole nitrate	160711M	1
Fagron	Miconazole nitrate	15I08-B07-314838	1
Fagron	Miconazole nitrate	15I08-B07-318686	2
Fagron	Miconazole nitrate	16E04-B03-322132	5
Fagron	Miconazole nitrate	1508-B07-318686	1
Fagron	Miconazole nitrate	2900/03/16	2
Fagron	Miconazole nitrate	15/08-B07-316911	1
Fagron	Miconazole nitrate	15I08-B07-215492	1
Fagron	Miconazole nitrate	16144702	1
Fagron	Miconazole nitrate	19041705	1
Fagron	Miconazole nitrate	16E04-B03-327367	1
Fagron	Miconazole nitrate	17C01-B02-334877	5
Fagron	Miconazole nitrate	16144725	2
Fagron	Miconazole nitrate	18B06-B03-345419	6
Fagron	Miconazole nitrate	17C01B02	1
Fagron	Miconazole nitrate	18B06-B03-345423	4
Fagron	Miconazole nitrate	18b06-b03-345419	1
Fagron	Miconazole nitrate	18B06-B03-345422	1
Fagron	Miconazole nitrate	29091808	1
Fagron	Miconazole nitrate	3248	1
Fagron	Miconazole nitrate	18C23-B02-248857	1
Fagron	Miconazole nitrate	1850000164	2
Fagron	Miconazole nitrate	18C23-B02-352488	1
Fagron	Miconazole nitrate	18c23-b02	1
Fagron	Miconazole nitrate	18c23-b02-352489	1
Fagron	Miconazole nitrate	1850003395	2
Fagron	Miconazole nitrate	19A31-B01-359397	1
Fagron	Miconazole nitrate	16E04-B03-327362	8
Fagron	Miconazole nitrate	16E04-B03	5
Fagron	Miconazole nitrate	18C23-B02-355295	3
Fagron	Miconazole nitrate	17C01-B02-335671	5
Fagron	Miconazole nitrate	18C23-B02-347802	2
Fagron	Miconazole nitrate	16E04-B03-330082	7
Fagron	Miconazole nitrate	18C23-B02-351310	5
Fagron	Miconazole nitrate	15108-b07-312321	1
Fagron	Miconazole nitrate	15A13-B07-308432	2
Fagron	Miconazole nitrate	15a13-b07-307140	1
Fagron	Miconazole nitrate	18b06-b03-345423	2
Fagron	Miconazole nitrate	19A31-b01-359392	1
Fagron	Miconazole nitrate	1811015-01	1
Fagron	Miconazole nitrate	17c01-b02-335671	1
Fagron	Miconazole nitrate	17c01-b02-334877	1
Fagron	Miconazole nitrate	19A31-B01-359392	2
Fagron	Miconazole nitrate	15A13-807	1
Fagron	Miconazole nitrate	18C23-B02-354469	2
Fagron	Miconazole nitrate	16E04-B03-332373	6
Fagron	Miconazole nitrate	18C23-B02-355707	2
Fagron	Miconazole nitrate	14B18-B02-291232	4
Fagron	Miconazole nitrate	15/08-b07-314838	2
Fagron	Miconazole nitrate	15/08-b07-318687	1
Fagron	Miconazole nitrate	17c01-b02-340778	1
Fagron	Miconazole nitrate	16e04-b03-322131	2
Fagron	Miconazole nitrate	1328-N06	1
Fagron	Miconazole nitrate	13A14-B09-287486	5
Fagron	Miconazole nitrate	18B06-B03-347788	3

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Miconazole nitrate	17C01-B02	2
Fagron	Miconazole nitrate	18B06-B03	3
Fagron	Miconazole nitrate	14D25-B06-299790	2
Fagron	Miconazole nitrate	15I08-B07-312321	1
Fagron	Miconazole nitrate	13A14B09283005	1
Fagron	Miconazole nitrate	13A14-B09-287453	1
Fagron	Miconazole nitrate	14D25-B06	4
Fagron	Miconazole nitrate	14H06-B01-299813	5
Fagron	Miconazole nitrate	15I08-B07-315492	1
Fagron	Miconazole nitrate	15/08-B07-315481	1
Fagron	Miconazole nitrate	14B18-B02-291248	6
Fagron	Miconazole nitrate	13A14-B09-287488	1
Fagron	Miconazole nitrate	14B18-B02-291250	1
Fagron	Miconazole nitrate	2900/04/14	2
Fagron	Miconazole nitrate	2900/16/14	4
Fagron	Miconazole nitrate	2900/09/16	3
Fagron	Miconazole nitrate	16E04-B03-322131	5
Fagron	Miconazole nitrate	14B18-B02-291249	1
Fagron	Miconazole nitrate	14B18-B02	4
Fagron	Miconazole nitrate	15A13-B07-307140	8
Fagron	Miconazole nitrate	15/08-B07-312317	1
Fagron	Miconazole nitrate	1316Q-03451	1
Fagron	Miconazole nitrate	15I08-B07-318485	2
Fagron	Miconazole nitrate	16144703	1
Fagron	Miconazole nitrate	17C01-B02-225671	1
Fagron	Miconazole nitrate	17C01-B02-334882	1
Fagron	Miconazole nitrate	18b06-b03-347788	1
Fagron	Miconazole nitrate	14D25-B06-294958	13
Fagron	Miconazole nitrate	15137905	1
Fagron	Miconazole nitrate	15I08-B07-315481	1
Fagron	Miconazole nitrate	17C01-B02-340778	7
Fagron	Miconazole nitrate	18C23-B02-350961	2
Fagron	Miconazole nitrate	18C23-B02-352489	2
Fagron	Miconazole nitrate	19A31-B01	1
Fagron	Miconazole nitrate	15/08-b07-315492	2
Fagron	Miconazole nitrate	16E04-B03-322124	12
Fagron	Miconazole nitrate	15I08-B07-31485	1
Fagron	Miconazole nitrate	18C23-B02-348857	1
Fagron	Miconazole nitrate	18C23-B02	5
Fagron	Miconazole nitrate	18C23-B02-353243	5
Fargon	Miconazole nitrate	14D25-B06-294959	1
Fargon	Miconazole nitrate	18B06-B03-345423	1
Faron	Miconazole nitrate	19A31-B01-359397	1
Fiebig	Miconazole nitrate	15/08-B07-314838	1
Fiebig	Miconazole nitrate	16144726	1
Fragon	Miconazole nitrate	18C23-B02-348857	1
Gehe	Miconazole nitrate	14149301	1
Gehe	Miconazole nitrate	13352811	1
Gehe	Miconazole nitrate	16144702	1
Gehe	Miconazole nitrate	16E04-B03-327362	1
Gehe	Miconazole nitrate	18B06-B03-345419	1
Gehe	Miconazole nitrate	18282105	1
GEHE	Miconazole nitrate	16144716	1
GEHE	Miconazole nitrate	18057903	1
Fagron	Miconazole nitrate	14B18-B02-291247	1
GEHE 13.05	Miconazole nitrate	14149311	1
Gehe 6.03.15	Miconazole nitrate	14149308	2
Gehe am 29.04.2014	Miconazole nitrate	13352802	4
Bombastus	Miconazole nitrate	15I08-B07-318686	1
Caelo	Miconazole nitrate	2900/10/14	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Miconazole nitrate	29001614	1
Caelo	Miconazole nitrate	2900/11/15	3
Caelo	Miconazole nitrate	16e04-b03-321367	1
Euro OTC	Miconazole nitrate	18057912	1
Fagron	Miconazole nitrate	16E04-B03-321354	3
Gehe/Ichthyol	Miconazole nitrate	16E04-B03-322132	1
gehe-06.11.18	Miconazole nitrate	18057906	1
Caelo	Miconazole nitrate	18282111	5
Hedinger	Miconazole nitrate	16144720	2
Hedinger	Miconazole nitrate	P2018/114	1
Herstellung	Miconazole nitrate	13185602	1
Ichthyol/Phoenix	Miconazole nitrate	16/098/M	1
Kehr	Miconazole nitrate	17C01-B02-334877	1
Noveda	Miconazole nitrate	18282105	1
Noweda	Miconazole nitrate	14149311	1
Noweda	Miconazole nitrate	14149310	1
Noweda	Miconazole nitrate	15137903	1
Noweda	Miconazole nitrate	16144704	1
Noweda	Miconazole nitrate	17217505	1
Noweda	Miconazole nitrate	1705039-02	1
Noweda	Miconazole nitrate	17217502	1
Noweda	Miconazole nitrate	18282109	1
Caelo	Miconazole nitrate	13352806	11
Noweda 10.12.2019	Miconazole nitrate	18282106	1
Noweda 26.11.2019	Miconazole nitrate	18282111	1
Euro OTC	Miconazole nitrate	16144701	1
Euro OTC	Miconazole nitrate	1409023-01	1
Euro OTC	Miconazole nitrate	170503901	1
Phoenix	Miconazole nitrate	13185611	1
Phoenix	Miconazole nitrate	13352801	1
Phoenix	Miconazole nitrate	15137915	1
Phoenix	Miconazole nitrate	15E04-B03-327367	1
Phoenix	Miconazole nitrate	17C01-B02-334882	1
Phoenix	Miconazole nitrate	18C23-B02-352489	1
Phoenix 21.10.14	Miconazole nitrate	14149301	1
PhoenixWE: 28.04.18 EK:...	Miconazole nitrate	17217505	1
phönix	Miconazole nitrate	15137907	1
phönix	Miconazole nitrate	16144701	2
phönix	Miconazole nitrate	16144716	1
Phönix	Miconazole nitrate	13H28-N06	1
Phönix	Miconazole nitrate	16E04-B03-322124	1
Phönix	Miconazole nitrate	16E04-B03-322131	1
Phönix	Miconazole nitrate	17217502	1
Phönix	Miconazole nitrate	3133	1
Phönix	Miconazole nitrate	18C23-B02-355707	1
Caelo	Miconazole nitrate	17217505	18
Sanacorp	Miconazole nitrate	12243801	1
Sanacorp	Miconazole nitrate	12243803	2
Sanacorp	Miconazole nitrate	13352801	1
Sanacorp EK:5,95 EUR...	Miconazole nitrate	16144703	1
Caelo	Miconazole nitrate	12243803	9
Sanacorp W.E:27.03.18 ...	Miconazole nitrate	16144726	2
Caelo	Miconazole nitrate	1/AD1	1
Caelo	Miconazole nitrate	AKD9	1
Caelo	Miconazole nitrate	8/AKD4	1
Caelo	Miconazole nitrate	13185601	4
Caelo	Miconazole nitrate	13352802	16
Caelo	Miconazole nitrate		3
Euro OTC	Miconazole nitrate	1307025-02	2
Fagron	Miconazole nitrate	13D22-N14	6

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Supplier	Substance	Batch	Spectra
Fagron	Miconazole nitrate	18C23-B02-356141	2
Fagron	Miconazole nitrate		1
Sanacorp	Miconazole nitrate		1

- 109 815 spectra from 742 *Apo-Ident* customers from a total of 31 579 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Miconazole nitrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Miconazole nitrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	499	0	110 190
Type B	0	723	0	118 419
Type C	0	1417	15	109 815

The substance/substance group *Miconazole nitrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7976 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.1701 %)
Type C	100.0000 % (> 99.8899 %)	98.9525 % (> 98.7430 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Miconazole nitrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	90.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Miconazole nitrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20875	21900	4.91	126.52
21649	21350	5.16	131.18
24593	22630	4.35	131.27
20817	21350	2.53	130.89
20905	21900	4.04	129.12
21350	21350	0.00	131.17
21900	21900	0.00	135.76
22630	22630	0.00	133.74
21351	21350	1.73	130.64

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Minoxidil**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20879-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Minoxidil; Minoxidilum

Special notes

When selecting the *Minoxidil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Minoxidil	7	10	343

Second-stage model

For differentiation of the substance/substance group *Minoxidil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Minoxidil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Minoxidil	13039501	20879	40	20130306
Caelo	Minoxidil	14093701	21359	40	20140428
Caelo	Minoxidil	14093701	21361	40	20140428
Euro OTC	Minoxidil	1311038-01	21630	59	AR-15-FG-007848-01
Euro OTC	Minoxidil	1411006-01	21912	60	20141210
Euro OTC	Minoxidil	1509035	21933	60	20151016*
Euro OTC	Minoxidil	1602013	22365	60	20160225*
Euro OTC	Minoxidil	1612011	22982	40	20170130*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 399 spectra of 8 reference samples from the substance/substance group *Minoxidil*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 290 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 620 spectra of 14 reference samples from the substance/substance group *Minoxidil*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Minoxidil	172278	23816	40
Caelo	Minoxidil	191957	24758	40
Euro OTC	Minoxidil	1607007	22688	40
Euro OTC	Minoxidil	1705008	23437	40
Euro OTC	Minoxidil	1710043	23896	40
Euro OTC	Minoxidil	1803004	24062	40
Euro OTC	Minoxidil	1807018-01	24190	40
Euro OTC	Minoxidil	1901005	24489	40
Euro OTC	Minoxidil	1907025	24803	40
Euro OTC	Minoxidil	2001035	25120	40
Euro OTC	Minoxidil	1411006-01	21912SI [†]	60
Euro OTC	Minoxidil	1509035	21933SI [†]	60
Euro OTC	Minoxidil	1602013	22365SI [†]	60
Euro OTC	Minoxidil	1612011	22982SI [†]	40

- 118522 spectra from a total of 2406 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1508 spectra from 381 *Apo-Ident* customers from 359 batches from the substance/substance group *Minoxidil*.
- Among them are spectra of independent samples from 324 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H.D	Minoxidil	1210056-01	1
AHC 14.08.13 EK40,14	Minoxidil	1210056-02	1
AHD	Minoxidil	1210056-01	1
AHD	Minoxidil	1311038-01	1
AHD	Minoxidil	15230812	1
AHD	Minoxidil	1504013-02	1
AHD	Minoxidil	18149801	1
Euro OTC	Minoxidil	1405028-01	29
Audor Pharma	Minoxidil	AP007/15M	4
Audor Pharma	Minoxidil	AP-016/15M	1
Alliance health	Minoxidil	1411006-01	3
Alliance Healthc. 15.05...	Minoxidil	1203035-03	1
Alliance Healthcare	Minoxidil	1210056-01	1
Alliance Healthcare	Minoxidil	1210056-02	1
anzag	Minoxidil	1504013-02	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Anzag	Minoxidil	1112024-02	1
Anzag	Minoxidil	13E13-N10	1
Anzag	Minoxidil	14234505	1
Anzag 14.11.12 ek:40,14	Minoxidil	120303501	1
Anzag 18.10.12 ek:40,14	Minoxidil	1203035-01	1
apo-ident.	Minoxidil	1607007-07	1
apomix	Minoxidil	1602013-01	1
Audor Pharma	Minoxidil	AP012/16M/5270	1
Audor Pharma	Minoxidil	AP088/14M	1
Audor Pharma	Minoxidil	8/14M	1
Audor Pharma	Minoxidil	AP006/17M	3
Audor Pharma	Minoxidil	AP011/16M	2
Audor Pharma	Minoxidil	AP020/11M	3
Audor Pharma	Minoxidil	AP010/12M	5
Audor Pharma	Minoxidil	AP006/13M	2
Audor Pharma	Minoxidil	APK007	1
Audor Pharma	Minoxidil	AP012/16M	4
Audor Pharma	Minoxidil	AP001/16M	7
Audor Pharma	Minoxidil	AP008/14M	6
Audor Pharma	Minoxidil	414E-02844	1
Audor Pharma	Minoxidil	AP016/15M	7
Bombastus	Minoxidil	1710043-01	1
Bombastus	Minoxidil	4/13	1
Bombastus	Minoxidil	1705008-01	2
Bombastus	Minoxidil	1112024-03	1
Caelo	Minoxidil	20160211-1	1
Caelo	Minoxidil	11K11-n09	1
Caelo	Minoxidil	11150207	1
Caelo	Minoxidil	11302003	1
Caelo	Minoxidil	12023902	1
Caelo	Minoxidil	11302005	1
Caelo	Minoxidil	12023901	2
Caelo	Minoxidil	1112024-01	1
Caelo	Minoxidil	12023907	4
Caelo	Minoxidil	20151112-5	1
Caelo	Minoxidil	12H07-N03	4
Caelo	Minoxidil	1203035	1
Caelo	Minoxidil	12023908	1
Caelo	Minoxidil	12273704	3
Caelo	Minoxidil	31051305	1
Caelo	Minoxidil	1309501	1
Caelo	Minoxidil	13039503	3
Caelo	Minoxidil	13E13-N10	1
Caelo	Minoxidil	13179504	2
Caelo	Minoxidil	12273710	1
Caelo	Minoxidil	13179503	6
Caelo	Minoxidil	13179502	5
Caelo	Minoxidil	130402901	1
Caelo	Minoxidil	22031402	1
Caelo	Minoxidil	14093707	1
Caelo	Minoxidil	14093703	4
Caelo	Minoxidil	14093702	2
Caelo	Minoxidil	1411006-01	2
Caelo	Minoxidil	14234505	5
Caelo	Minoxidil	14234502	2
Caelo	Minoxidil	14L03-B02-301431	1
Caelo	Minoxidil	5081502	1
Caelo	Minoxidil	15E19-B06-308182	1
Caelo	Minoxidil	8719	1
Caelo	Minoxidil	15230802	3

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Supplier	Substance	Batch	Spectra
Caelo	Minoxidil	17011602	1
Caelo	Minoxidil	1509035-01	3
Caelo	Minoxidil	15230805	2
Caelo	Minoxidil	15230803	3
Caelo	Minoxidil	2827	1
Caelo	Minoxidil	15K17-B06-321926	1
Caelo	Minoxidil	121005601	1
Caelo	Minoxidil	15436204	2
Caelo	Minoxidil	15K17-B05-318692	1
Caelo	Minoxidil	15230806	2
Caelo	Minoxidil	15436406	4
Caelo	Minoxidil	15436412	1
Caelo	Minoxidil	5217M-02844	1
Caelo	Minoxidil	17227801	12
Caelo	Minoxidil	17227803	9
Caelo	Minoxidil	17H08-B06-342282	1
Caelo	Minoxidil	1807018-01	6
Caelo	Minoxidil	18016103	1
Caelo	Minoxidil	18016107	3
Caelo	Minoxidil	18016112	1
Caelo	Minoxidil	1901005-01	1
Caelo	Minoxidil	18149810	2
Caelo	Minoxidil	18149815	2
Caelo	Minoxidil	13I23-N07	2
Fagron	Minoxidil	16j24-B04-329291	1
Caelo	Minoxidil	1520002455	1
Caelo	Minoxidil	1705008-01	4
Caelo	Minoxidil	13/23-N07	1
Caelo	Minoxidil	13K04B05290380	1
Caelo	Minoxidil	1607007-01	2
Caelo	Minoxidil	1807018_01	1
Caelo	Minoxidil	13179501	2
Caelo	Minoxidil	12273703	2
Caelo	Minoxidil	1210056-01	2
Caelo	Minoxidil	1210056-02	3
Caelo	Minoxidil	1509035	1
Caelo	Minoxidil	170043-01	1
Caelo	Minoxidil	17H08-B06-341377	1
Caelo	Minoxidil	1602013-01	9
Caelo	Minoxidil	130402902	1
Caelo	Minoxidil	1504013-01	5
Caelo	Minoxidil	1311038-01	2
Caelo	Minoxidil	1405028-01	1
Caelo	Minoxidil	15230804	6
Caelo	Minoxidil	160201302	2
Caelo	Minoxidil	13179507	3
Caelo	Minoxidil	3013M-02844	1
Caelo	Minoxidil	14234509	3
Caelo	Minoxidil	1710043-01	7
Caelo	Minoxidil	15436408	3
Caelo	Minoxidil	1203035-01	1
Caelo	Minoxidil	13373106	1
Caelo	Minoxidil	15230811	4
Caelo	Minoxidil	15436202	7
Caelo	Minoxidil	15436201	5
Caelo	Minoxidil	160707-01	1
Caelo	Minoxidil	15436404	3
Caelo	Minoxidil	15H07-B03-317340	1
Caelo	Minoxidil	15436414	5
Caelo	Minoxidil	15230812	1

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Supplier	Substance	Batch	Spectra
Caelo	Minoxidil	18149802	7
Caelo	Minoxidil	15436415	1
Caelo	Minoxidil	2905047-01	1
Caelo	Minoxidil	16J24-B05-332092	1
Caelo	Minoxidil	1504013-02	1
Caelo	Minoxidil	15E19-B06-309180	1
Caelo	Minoxidil	15K17-B05-318240	1
Caelo	Minoxidil	15k17-b06-324965	1
Caelo	Minoxidil	170500801	4
Caelo	Minoxidil	18149801	1
Caelo	Minoxidil	K0071/16/04/065	1
Caelo	Minoxidil	13179501-3467312121	1
Caelo	Minoxidil	14093706	3
Caelo	Minoxidil	1803004-01	3
Caelo	Minoxidil	15E19-B06-308183	1
Caesar & Loretz GmbH	Minoxidil	13039501	1
Caesar & Loretz GmbH	Minoxidil	18149802	1
Caesar & Loretz GmbH	Minoxidil	18149810	1
Caesar & Loretz GmbH / ...	Minoxidil	14093702	1
Caesar & Loretz GmbH / ...	Minoxidil	14234505	1
Doppeleiche Apotheke	Minoxidil	13E13-N10	2
Eurho	Minoxidil	1803004-01	2
EuRho	Minoxidil	1105030-02	1
EuRho	Minoxidil	1108039-02	2
EuRho	Minoxidil	1705008-01	1
EuRho	Minoxidil	1710043-01	2
EuRho / Noweda	Minoxidil	1304029-02	1
EuRho/ Alliance	Minoxidil	1705008-01	1
EuRho/Fiebig	Minoxidil	1411006-01	1
EuRho/Kehr	Minoxidil	30/17	1
EuRho/Kehr	Minoxidil	1803004-01	2
EuRho/Noweda	Minoxidil	1607007-01	1
EuRho/Noweda	Minoxidil	1710043-01	2
EuRho/Sanacorp	Minoxidil	1901005-01	1
Euro	Minoxidil	1304029-02	1
Euro	Minoxidil	1504013-01	2
Euro OT/Phönix	Minoxidil	1710043-01	1
Euro OTC	Minoxidil	1203035	1
Euro OTC	Minoxidil	160700701	3
Euro OTC	Minoxidil	1203035-03	11
Euro OTC	Minoxidil	130402902	1
Euro OTC	Minoxidil	130402901	1
Euro OTC	Minoxidil	1304029-C2	1
Euro OTC	Minoxidil	131103801	4
Euro OTC	Minoxidil	29071402	1
Euro OTC	Minoxidil	700158	1
Euro OTC	Minoxidil	141100601	5
Euro OTC	Minoxidil	1504013-2	1
Euro OTC	Minoxidil	1602016-01	1
Euro OTC	Minoxidil	1612011-01	59
Euro OTC	Minoxidil	15436404	1
Euro OTC	Minoxidil	2091714	1
Euro OTC	Minoxidil	1710043-01	56
Euro OTC	Minoxidil	16120-01	1
Euro OTC	Minoxidil	171004301	5
Euro OTC	Minoxidil	17H08-B06	1
Euro OTC	Minoxidil	15081829	1
Euro OTC	Minoxidil	1807018-01	31
Euro OTC	Minoxidil	103004-01	1
Euro OTC	Minoxidil	1907025-01	6

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Supplier	Substance	Batch	Spectra
Euro OTC	Minoxidil	1112024-02	5
Euro OTC	Minoxidil	16070007-01	1
Euro OTC	Minoxidil	1203035-01	10
Euro OTC	Minoxidil	161201-01	1
Euro OTC	Minoxidil	170703M/1602013-02	1
Euro OTC	Minoxidil	1803004_01	1
Euro OTC	Minoxidil	1907025_01	1
Euro OTC	Minoxidil	140502801	3
Euro OTC	Minoxidil	1705008_01	1
Euro OTC	Minoxidil	1901005-01	24
Euro OTC	Minoxidil	1803004-01	29
Euro OTC	Minoxidil	1112024-01	1
Euro OTC	Minoxidil	121005601	1
Euro OTC	Minoxidil	104029-02	1
Euro OTC	Minoxidil	1602013-01	35
Euro OTC	Minoxidil	1607007	1
Euro OTC	Minoxidil	1612011-011	1
Euro OTC	Minoxidil	1710043_01	1
Euro OTC	Minoxidil	1707018-01	1
Euro OTC	Minoxidil	1108039-03	1
Euro OTC	Minoxidil	1304029-02	15
Euro OTC	Minoxidil	180708-01	1
Euro OTC	Minoxidil	4/13	2
Euro OTC	Minoxidil	1705008-01	39
Euro OTC	Minoxidil	1710043-03	1
Euro OTC	Minoxidil	180701801	1
Euro OTC	Minoxidil	1405028-1	1
Euro OTC	Minoxidil	1102010-02	1
Euro OTC	Minoxidil	1210056-01	14
Euro OTC	Minoxidil	1210056-02	25
Euro OTC	Minoxidil	1304029-01	16
Euro OTC	Minoxidil	1919	1
Euro OTC	Minoxidil	14050281	1
Euro OTC	Minoxidil	12/17	1
Euro OTC	Minoxidil	13001	1
Euro OTC	Minoxidil	1602013-1	1
Euro OTC	Minoxidil	190100501	1
Euro OTC	Minoxidil	12/16	2
Euro OTC	Minoxidil	13110838-01	1
Euro OTC	Minoxidil	1108039-01	1
Euro OTC	Minoxidil	1112024-03	3
Euro OTC	Minoxidil	1203035-02	6
Euro OTC	Minoxidil	120303503	1
Euro OTC	Minoxidil	17050008	1
Euro OTC	Minoxidil	180300401	3
Euro OTC	Minoxidil	1509035-01	36
Euro OTC	Minoxidil	1504013-01	29
Euro OTC	Minoxidil	17100-43-01	1
Euro OTC	Minoxidil	6/12	2
Euro OTC	Minoxidil	1607001-01	1
Euro/ Phönix	Minoxidil	1405028-01	1
EUro/AHD	Minoxidil	1203035-03	2
Euro/Anzag	Minoxidil	150903501	1
Euro/Gehe	Minoxidil	1112024-03	1
Euro/Gehe	Minoxidil	140528-01	1
Euro/Noweda	Minoxidil	1602013-02	1
Euro/Noweda	Minoxidil	1612011-01	1
Euro OTC	Minoxidil	16122011_01	1
Euro/Phönix	Minoxidil	161201101	2
Euro/Phönix	Minoxidil	1901005	1

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Supplier	Substance	Batch	Spectra
euroct/Gehe	Minoxidil	1304029-01	1
Euro OTC	Minoxidil	1504013-02	24
Euro OTC	Minoxidil	1607007-01	30
Euro OTC	Minoxidil	160201301	1
Euro OTC	Minoxidil	1803004	1
Euro OTC	Minoxidil	1009042-01	3
Euro OTC	Minoxidil	161201101	1
Euro OTC	Minoxidil	12100056-01	1
Euro OTC	Minoxidil	140528-01	1
Euro OTC	Minoxidil	150401-01	1
Euro OTC	Minoxidil	19/16	1
Euro OTC	Minoxidil	1807018-02	1
Euro OTC	Minoxidil	10/13	1
europarm/gehe	Minoxidil	1710043-01	1
Europarm/Sanacorp	Minoxidil	1210056-01	1
EurPS	Minoxidil	1504013-01	2
Fagrin	Minoxidil	15K17-B06-321926	1
Fagron	Minoxidil	14L03-B02-301431	1
Fagron	Minoxidil	11K11-N09	3
Fagron	Minoxidil	4110I-02844	1
Fagron	Minoxidil	612212844	1
Fagron	Minoxidil	12C29-N05	5
Fagron	Minoxidil	12H07-N03	12
Fagron	Minoxidil	120303503	1
Fagron	Minoxidil	11H07-N03	1
Fagron	Minoxidil	12H07N03	1
Fagron	Minoxidil	12C29-N050087/240	1
Fagron	Minoxidil	12H07-N030265/432	1
Fagron	Minoxidil	12H07-No3	1
Fagron	Minoxidil	27081301	1
Fagron	Minoxidil	13E13N10	1
Fagron	Minoxidil	26111302	1
Fagron	Minoxidil	13I23-N07	8
Fagron	Minoxidil	11021402	1
Fagron	Minoxidil	13J29-B02	1
Fagron	Minoxidil	13J23N07	2
Fagron	Minoxidil	13K04-B05-290377	5
Fagron	Minoxidil	1311038-01	1
Fagron	Minoxidil	13K04-B05-290379	2
Fagron	Minoxidil	13K04-B05-290380	3
Fagron	Minoxidil	14B04-B07	1
Fagron	Minoxidil	14B04-B07-297364	1
Fagron	Minoxidil	14L03-B02-301541	1
Fagron	Minoxidil	1411006-01	2
Fagron	Minoxidil	14L03-B02-301430	1
Fagron	Minoxidil	1504013-01	2
Fagron	Minoxidil	15E19-B06-308182	5
Fagron	Minoxidil	14L03-B02301434	1
Fagron	Minoxidil	14L03-B02301429	1
Fagron	Minoxidil	15F02-B08	1
Fagron	Minoxidil	14L03-B02-30129	1
Fagron	Minoxidil	14L03-B02	2
Fagron	Minoxidil	15E19-B06-308183	6
Fagron	Minoxidil	15E19-B06-308181	5
Fagron	Minoxidil	14L03-B02-301428	1
Fagron	Minoxidil	15E19-B06-308183	1
Fagron	Minoxidil	15F02-B09-312663	2
Fagron	Minoxidil	15E19-B09-308181	1
Fagron	Minoxidil	1510001251	3
Fagron	Minoxidil	15K17-B05-318241	1

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Supplier	Substance	Batch	Spectra
Fagron	Minoxidil	15H07-B01-314726	1
Fagron	Minoxidil	15K197-B05-318411	1
Fagron	Minoxidil	15K17-B06-325490	2
Fagron	Minoxidil	15K17-B06-321928	2
Fagron	Minoxidil	15K17-B06	1
Fagron	Minoxidil	1612011-01	1
Fagron	Minoxidil	17B22-B01-334447	1
Fagron	Minoxidil	15436408	1
Fagron	Minoxidil	16J24-B05	1
Fagron	Minoxidil	17B22-B01-335427	4
Fagron	Minoxidil	17B22-B02-336690	1
Fagron	Minoxidil	1705008-01	1
Fagron	Minoxidil	17B22-B02	1
Fagron	Minoxidil	17H08-B06	1
Fagron	Minoxidil	5/17M	1
Fagron	Minoxidil	18C19-B01-348984	3
Fagron	Minoxidil	15K17-B05-318692	1
Fagron	Minoxidil	17H08-B09	1
Fagron	Minoxidil	18008	1
Fagron	Minoxidil	15K17-B05-318691	2
Fagron	Minoxidil	13K04-B05-0004	1
Fagron	Minoxidil	12H07-N03	1
Fagron	Minoxidil	12C29-N050145/240	1
Fagron	Minoxidil	13123-N07	1
Fagron	Minoxidil	14L03-B02-301429	6
Fagron	Minoxidil	15e19-b06-308180	1
Fagron	Minoxidil	15K17-B05-320188	3
Fagron	Minoxidil	15K17-B06-324965	2
Fagron	Minoxidil	15K17-B06-321927	3
Fagron	Minoxidil	15K17-B06-321926	5
Fagron	Minoxidil	18C27-B01-354525	2
Fagron	Minoxidil	17B22-B02-336689	3
Fagron	Minoxidil	17B22/B02/336689	2
Fagron	Minoxidil	18C20-B01	1
Fagron	Minoxidil	15E19-06-308183	1
Fagron	Minoxidil	18C19-B01-348985	1
Fagron	Minoxidil	11E17-N07	1
Fagron	Minoxidil	18C20-B01-352629	3
Fagron	Minoxidil	1520002631	1
Fagron	Minoxidil	17H08-B06-340514	2
Fagron	Minoxidil	18C20-B01-351844	3
Fagron	Minoxidil	14B04-B07-290883	3
Fagron	Minoxidil	15K17-B05-318240	1
Fagron	Minoxidil	2/16M	3
Fagron	Minoxidil	18C27-B01-354524	2
Fagron	Minoxidil	1901005-01	1
Fagron	Minoxidil	17H08-B09-346948	1
Fagron	Minoxidil	321926	1
Fagron	Minoxidil	16J24-B04-329291	1
Fagron	Minoxidil	13E13-N10	9
Fagron	Minoxidil	15E19-B06	1
Fagron	Minoxidil	17B22-B01	2
Fagron	Minoxidil	12A25-N04	4
Fagron	Minoxidil	12H07-N03	1
Fagron	Minoxidil	1420001962	1
Fagron	Minoxidil	16J24-B04-328218	4
Fagron	Minoxidil	1/16M	2
Fagron	Minoxidil	17B22-B02-338767	1
Fagron	Minoxidil	7/13	1
Fagron	Minoxidil	16J24-B05-332093	2

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Supplier	Substance	Batch	Spectra
Fagron	Minoxidil	17H08-B06-341377	5
Fagron	Minoxidil	13H07-N03	1
Fagron	Minoxidil	15E19-B06-308179	1
Fagron	Minoxidil	170612184	1
Fagron	Minoxidil	17H08-B09-346945	1
Fagron	Minoxidil	18C20-b01-351844	1
Fagron	Minoxidil	18C20-B01-352702	1
Fagron	Minoxidil	19b18-b06-191023	1
Fagron	Minoxidil	14L03-B02-301430	2
Fagron	Minoxidil	16J24-B05-332092	3
Fagron	Minoxidil	18C20-B01-352116	1
Fagron	Minoxidil	1803004-01	2
Fagron	Minoxidil	1210056-02	1
Fagron	Minoxidil	15E19-B06-308180	5
Fagron	Minoxidil	15K17-B05-318411	2
Fagron	Minoxidil	15K17-B06-325491	2
Fagron	Minoxidil	16J24-B04-328226	3
Fagron	Minoxidil	1520000768	2
Fagron	Minoxidil	17H08-B06-341376	5
Fagron	Minoxidil	19B21-B07-190615	1
Fiebig	Minoxidil	1509035-01	1
Fiebig	Minoxidil	1607007-01	1
Fiebig	Minoxidil	1612011-01	1
Fiebig	Minoxidil	1705008-01	1
Fiebig	Minoxidil	171004301	1
Fiebig	Minoxidil	1807017-01	1
Fiebig	Minoxidil	1901005-01	1
Fiebig ek: 36.06EUR 31.0812	Minoxidil	111202403	1
Gatt-Koller	Minoxidil	1803103	2
Gehe	Minoxidil	AP006/13M	1
Gehe	Minoxidil	1405028-01	1
Gehe	Minoxidil	1602013-01	1
Gehe	Minoxidil	15436406	1
Gehe	Minoxidil	15436201	1
Gehe	Minoxidil	1612011-01	1
Gehe	Minoxidil	1705008-01	1
Gehe	Minoxidil	1710043-01	1
GEHE	Minoxidil	1907025-01	1
Gehe / EuRho	Minoxidil	1803004-01	1
Caelo	Minoxidil	150401301	1
Audor Pharma	Minoxidil	APK0071/16/04/065-1M	1
Caelo	Minoxidil	160013-01	1
Caelo	Minoxidil	AP011/16M	1
Caelo	Minoxidil	15436202/1060217	1
Caelo	Minoxidil	1070318/17227803	1
Caelo	Minoxidil	1602013-02	3
Gehe/Euro	Minoxidil	150903501	1
Euro OTC	Minoxidil	6614849	1
Hedinger	Minoxidil	14B04-B07	2
Hedinger/Fiebig	Minoxidil	1612011-01	1
Hedinger/Sanacorp	Minoxidil	12C29-N05	1
Ichthyol/Noweda	Minoxidil	17117803	1
Ichthyol-Gesellschaft	Minoxidil	1311038-01	1
ICROM	Minoxidil	6/12	1
icrom spa	Minoxidil	511v	1
Icrom/Gehe	Minoxidil	1602013-01	1
Jenne	Minoxidil	17H08-B06-341377	1
Jenne	Minoxidil	P2019/93	1
Kehr	Minoxidil	1705008-01	1
Kehr	Minoxidil	1803004-01	1

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Supplier	Substance	Batch	Spectra
Krieger	Minoxidil	171004301	1
Fagron	Minoxidil	16/24-B04-328218	1
Caelo	Minoxidil	AP006/17M	1
Noweda	Minoxidil	14093703	1
Noweda/ Infecto Pharm	Minoxidil	1607007-01	1
Noweda/Apomix	Minoxidil	1504013-02	1
Caelo	Minoxidil	16J24-B05-331128	1
Euro OTC	Minoxidil	2002312844	1
Euro OTC	Minoxidil	1411006601	1
Phoenix	Minoxidil	1602013-02	1
Phoenix	Minoxidil	3057	1
Phoenix	Minoxidil	16J25-B05-332092	1
Phoenix	Minoxidil	3399	1
PhOENIX 19.03.2012	Minoxidil	1311038-01	2
Caelo	Minoxidil	18149813	2
phönix	Minoxidil	1509035-01	1
phönix	Minoxidil	1602013-01	3
phönix	Minoxidil	1612011-01	2
Phönix	Minoxidil	1112024-03	1
Phönix	Minoxidil	1304029-01	1
Phönix	Minoxidil	1203035-02	1
Phönix	Minoxidil	1602013-02	1
Phönix	Minoxidil	1612011-01	1
Phönix	Minoxidil	1705008-01	1
Phönix	Minoxidil	1901005-01	1
Phönix	Minoxidil	19B21-B07-190661	1
Phönix	Minoxidil	1907025-01	2
PHÖNIX	Minoxidil	1705008-01	2
Phönix /euro	Minoxidil	170500801	2
Caelo	Minoxidil	180701801	1
Caelo	Minoxidil	14062018-RQ-A	1
Phönix/EuRho	Minoxidil	1710043-01	2
Euro OTC	Minoxidil	1807018	1
Euro OTC	Minoxidil	170500801	3
sanacorp	Minoxidil	1405028-01	1
sanacorp	Minoxidil	13K04-B05-290379	1
Sanacorp	Minoxidil	1203035-01	1
Sanacorp	Minoxidil	1210056-01	1
Sanacorp	Minoxidil	120056-01	1
Sanacorp	Minoxidil	1210056-02	2
Sanacorp	Minoxidil	13179502	2
Sanacorp	Minoxidil	13179501	2
Sanacorp	Minoxidil	1304029-02	3
Sanacorp	Minoxidil	14093701	1
Sanacorp	Minoxidil	1405028-01	1
Sanacorp	Minoxidil	14093702	1
Sanacorp	Minoxidil	140502801	1
Sanacorp	Minoxidil	1411006-01	1
Sanacorp	Minoxidil	1504013-01	1
Sanacorp	Minoxidil	1612011-01	1
Sanacorp, 81,00EUR, 27.1.17	Minoxidil	1607007-01	1
Caelo	Minoxidil	11e17-n07	1
Fagron	Minoxidil	17B22-B02-338766	2
Caelo	Minoxidil	11150209	1
Euro OTC	Minoxidil	1602013-02	12
Spangro 1.10.19	Minoxidil	16J24-B04-328224	1
Spangro 25.1.2014	Minoxidil	13/23-N07	1
Th. Geyer	Minoxidil	1602013-01	1
Vdl 14.07.14	Minoxidil	1311038-01	1
VDL;81,0EUR;21.05.15	Minoxidil	1411006-01	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Minoxidil	1311038-01	30
Euro OTC	Minoxidil	1411006-01	39
Audor Pharma	Minoxidil		40
Caelo	Minoxidil	13039501	7
Caelo	Minoxidil		7
Euro OTC	Minoxidil	1612011	1
Euro OTC	Minoxidil		8
Kumar Organic Products ...	Minoxidil		1
phönix	Minoxidil		1

- 109 739 spectra from 742 *Apo-Ident* customers from a total of 31 539 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Minoxidil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Minoxidil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	381	18	110 290
Type B	0	616	4	118 522
Type C	0	1500	8	109 739

The substance/substance group *Minoxidil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	95.4887 % (> 94.7368 %)
Type B	100.0000 % (> 99.9893 %)	99.3548 % (> 98.8710 %)
Type C	100.0000 % (> 99.8899 %)	99.4695 % (> 99.2706 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Minoxidil* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium citrate tetrahydrate	29.70	—
Bacitracin	31.27	—
Magnesium citrate	51.80	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Minoxidil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20879	21630	3.84	33.86
21359	21630	3.66	32.98
21361	21630	3.02	33.68
21630	21630	0.00	34.59
21912	21933	3.03	31.14
21933	21933	0.00	29.70
22365	22365	0.00	34.92
22982	22982	0.00	36.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Mometasone furoate, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20100-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mometasone furoate, micronized; Mometasoni furoas micronisatum

Special notes

When selecting the *Mometasone furoate, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mometasone furoate, micronized	7	6	296

Second-stage model

For differentiation of the substance/substance group *Mometasone furoate, micronized* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mometasone furoate, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Mometasone furoa...	160286	22433	60	20160316*
Caelo	Mometasone furoa...	163532	23046	40	20170104*
Euro OTC	Mometasone furoa...	1403015-01	21602	60	20140503
Euro OTC	Mometasone furoa...	1403015-01	21602SI	31	20140503
Euro OTC	Mometasone furoa...	1510036	22238	60	20151118*
Euro OTC	Mometasone furoa...	1510036	22238SI	30	20151118*
Euro OTC	Mometasone furoa...	1610009	23136	40	20170321*
Fagron	Mometasone furoa...	13F17-N01	20850	40	20130620
Fagron	Mometasone furoa...	13F17-N01	20850SI	44	20130620
Fagron	Mometasone furoa...	16A20-B06-319750	22887	40	20160209
Fagron	Mometasone furoa...	16A20-B06-319750	22887SI	30	20160209

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 475 spectra of 11 reference samples from the substance/substance group *Mometasone furoate, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 214 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 496 spectra of 15 reference samples from the substance/substance group *Mometasone furoate, micronized*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Mometasone furoate, micronized	13304605	21374	60
Caelo	Mometasone furoate, micronized	183341	24563	40
Euro OTC	Mometasone furoate, micronized	1606021	22715	40
Euro OTC	Mometasone furoate, micronized	1711027	23878	40
Euro OTC	Mometasone furoate, micronized	1810008	24295	40
Euro OTC	Mometasone furoate, micronized	1906035	24794	40
Caelo	Mometasone furoate, micronized	13304605	21374SI	38
Caelo	Mometasone furoate, micronized	160286	22433SI [†]	30
Caelo	Mometasone furoate, micronized	163532	23046SI [†]	23
Caelo	Mometasone furoate, micronized	183341	24563SI	21
Euro OTC	Mometasone furoate, micronized	1606021	22715SI	33
Euro OTC	Mometasone furoate, micronized	1610009	23136SI [†]	20
Euro OTC	Mometasone furoate, micronized	1711027	23878SI	27
Euro OTC	Mometasone furoate, micronized	1810008	24295SI	20
Euro OTC	Mometasone furoate, micronized	1906035	24794SI	24

- 118646 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1075 spectra from 333 *Apo-Ident* customers from 320 batches from the substance/substance group *Mometasone furoate, micronized*.
- Among them are spectra of independent samples from 296 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Ador Pharma	Mometasone furoate, micronized	APMOM006/0517M	1
AHD 20.06.14 EK 37,29	Mometasone furoate, micronized	12C07-B05-291268	1
Fagron	Mometasone furoate, micronized	15G08-B11-312233	4
Fagron	Mometasone furoate, micronized	15I11-B02-314479	4
Fagron	Mometasone furoate, micronized	15G08-B11-317182	8
Alliance Health 27.01.2...	Mometasone furoate, micronized	13J23-N02	1
Alte Apotheke	Mometasone furoate, micronized	1606021-01	1
Anzag	Mometasone furoate, micronized	12J29N03	1
Anzag	Mometasone furoate, micronized	13D08-N06	1
Audor Pharma	Mometasone furoate, micronized	APMOM006/0117M	4
Audor Pharma	Mometasone furoate, micronized	APMOM010/0116M	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Audor Pharma	Mometasone furoate, micronized	APMOM006/0177M	1
Audor Pharma	Mometasone furoate, micronized	APMOM301/0118-1M	1
Audor Pharma	Mometasone furoate, micronized	APMOM006/0517M	5
Audor Pharma	Mometasone furoate, micronized	APMOM301/0118M	2
Bombastus	Mometasone furoate, micronized	16J24-B11-335793	1
Bombastus	Mometasone furoate, micronized	18B19-B07-352632	1
Cael Sanacorp 05.02.2016	Mometasone furoate, micronized	14H06-B07-298481	1
Caelo	Mometasone furoate, micronized	12351202	1
Caelo	Mometasone furoate, micronized	13304612	1
Caelo	Mometasone furoate, micronized	15b11b03	1
Caelo	Mometasone furoate, micronized	12035608	2
Caelo	Mometasone furoate, micronized	12351205	2
Caelo	Mometasone furoate, micronized	12035607	2
Caelo	Mometasone furoate, micronized	18102013B	1
Caelo	Mometasone furoate, micronized	12351210	1
Caelo	Mometasone furoate, micronized	13H13-N04	1
Caelo	Mometasone furoate, micronized	13H13N04	1
Caelo	Mometasone furoate, micronized	13304603	1
Caelo	Mometasone furoate, micronized	14E20-B04	1
Caelo	Mometasone furoate, micronized	12351208	1
Caelo	Mometasone furoate, micronized	NU0698M	1
Caelo	Mometasone furoate, micronized	13304609	1
Caelo	Mometasone furoate, micronized	14H06-B07298481	1
Caelo	Mometasone furoate, micronized	200315A	1
Caelo	Mometasone furoate, micronized	14281102	3
Caelo	Mometasone furoate, micronized	14281101	2
Caelo	Mometasone furoate, micronized	15B11-B03-304121	2
Caelo	Mometasone furoate, micronized	15189802	5
Caelo	Mometasone furoate, micronized	15G08-B11-310865	1
Caelo	Mometasone furoate, micronized	15189801	2
Caelo	Mometasone furoate, micronized	15189807	5
Caelo	Mometasone furoate, micronized	15279004	4
Caelo	Mometasone furoate, micronized	16028609	6
Caelo	Mometasone furoate, micronized	16028607	8
Caelo	Mometasone furoate, micronized	15/11-B02-314479	1
Caelo	Mometasone furoate, micronized	16A20-B06-319748	1
Caelo	Mometasone furoate, micronized	16A20-B06-319749	1
Caelo	Mometasone furoate, micronized	2885	1
Caelo	Mometasone furoate, micronized	16C24_B03_324852	2
Caelo	Mometasone furoate, micronized	16C24-B03-324852	1
Caelo	Mometasone furoate, micronized	16028604	4
Caelo	Mometasone furoate, micronized	MOM010/0116	3
Caelo	Mometasone furoate, micronized	16181709	1
Caelo	Mometasone furoate, micronized	16028605	2
Caelo	Mometasone furoate, micronized	16181705	4
Caelo	Mometasone furoate, micronized	16353201	6
Caelo	Mometasone furoate, micronized	1704012A	1
Caelo	Mometasone furoate, micronized	16181715	8
Caelo	Mometasone furoate, micronized	16353204	2
Caelo	Mometasone furoate, micronized	16353206	11
Caelo	Mometasone furoate, micronized	16J24-B11-335793	1
Caelo	Mometasone furoate, micronized	1635209	1
Caelo	Mometasone furoate, micronized	17348901	6
Caelo	Mometasone furoate, micronized	16C24-B03-328272	1
Caelo	Mometasone furoate, micronized	1711027-01	1
Caelo	Mometasone furoate, micronized	18026006	4
Caelo	Mometasone furoate, micronized	18026008	2
Caelo	Mometasone furoate, micronized	18B19-B07-351351	1
Caelo	Mometasone furoate, micronized	18026017	3
Caelo	Mometasone furoate, micronized	18334104	7

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Mometasone furoate, micronized	18334106	1
Caelo	Mometasone furoate, micronized	16353209	18
Caelo	Mometasone furoate, micronized	18334101	5
Caelo	Mometasone furoate, micronized	17D19-B02-342643	2
Caelo	Mometasone furoate, micronized	18026015	1
Caelo	Mometasone furoate, micronized	701834-0002	1
Caelo	Mometasone furoate, micronized	15189804	3
Caelo	Mometasone furoate, micronized	15G08-B11-310864	2
Caelo	Mometasone furoate, micronized	17D19-B02	1
Caelo	Mometasone furoate, micronized	16J24-B11-332112	1
Caelo	Mometasone furoate, micronized	18334110	3
Caelo	Mometasone furoate, micronized	18026004	11
Caelo	Mometasone furoate, micronized	1711027	1
Caelo	Mometasone furoate, micronized	1810008-01	1
Caelo	Mometasone furoate, micronized	19200603	1
Caelo	Mometasone furoate, micronized	15B11B03304122	1
Caelo	Mometasone furoate, micronized	16181714	1
Caelo	Mometasone furoate, micronized	18334108	4
Caelo	Mometasone furoate, micronized	MOM001/0317	1
Caelo	Mometasone furoate, micronized	15G08-B11-317182	1
Caelo	Mometasone furoate, micronized	18026009	2
Caelo	Mometasone furoate, micronized	1602809	1
Caelo	Mometasone furoate, micronized	18026012	6
Caelo	Mometasone furoate, micronized	NT1568M	1
Caelo	Mometasone furoate, micronized	13F27-N02	1
Caelo	Mometasone furoate, micronized	12351215	4
Caelo	Mometasone furoate, micronized	13304606	2
Caelo	Mometasone furoate, micronized	14e20-b04-291267	1
Caelo	Mometasone furoate, micronized	N01352M	1
Caelo	Mometasone furoate, micronized	14E20-B04-291267	1
Caelo	Mometasone furoate, micronized	16028606	6
Caelo	Mometasone furoate, micronized	16181704	5
Caelo	Mometasone furoate, micronized	16J24-B11	1
Caelo	Mometasone furoate, micronized	16353210	1
Caelo	Mometasone furoate, micronized	18026003	1
Caelo	Mometasone furoate, micronized	19200605	1
Caelo	Mometasone furoate, micronized	192006004	1
Caelo	Mometasone furoate, micronized	240913a	1
Caelo	Mometasone furoate, micronized	13J23-N02	1
Caelo	Mometasone furoate, micronized	14C07-B05-291268	8
Caelo	Mometasone furoate, micronized	15G08-B11-322739	1
Caelo	Mometasone furoate, micronized	1635206	1
Caelo	Mometasone furoate, micronized	18026001	15
Caelo	Mometasone furoate, micronized	17D19-B02-339277	1
Caelo	Mometasone furoate, micronized	18026011	15
Caelo	Mometasone furoate, micronized	15189806	1
Caelo	Mometasone furoate, micronized	APMOM006/0117M	1
Caelo	Mometasone furoate, micronized	1635211	1
Caelo	Mometasone furoate, micronized	18334102	5
Caelo	Mometasone furoate, micronized	19200601	1
Caelo	Mometasone furoate, micronized	1510036-001	1
Caelo	Mometasone furoate, micronized	15189809	4
Caelo	Mometasone furoate, micronized	15/11-Bo2-314479	1
Caelo	Mometasone furoate, micronized	NV1000M	1
Caelo	Mometasone furoate, micronized	16353205	3
Caelo	Mometasone furoate, micronized	1610009-01	4
Caelo	Mometasone furoate, micronized	16353207	11
Caelo	Mometasone furoate, micronized	16353211	11
Caelo	Mometasone furoate, micronized	18026007	5
Caelo	Mometasone furoate, micronized	16028602	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Mometasone furoate, micronized	12351207	1
Caelo	Mometasone furoate, micronized	12339604	1
Caelo	Mometasone furoate, micronized	13304604	2
Caelo	Mometasone furoate, micronized	15110305	4
Caelo	Mometasone furoate, micronized	16181710	2
Caelo	Mometasone furoate, micronized	16353208	4
Caelo	Mometasone furoate, micronized	18B19B07-351001	1
Caelo	Mometasone furoate, micronized	16028601	3
Caeo	Mometasone furoate, micronized	12351201	1
Caeo/Noweda	Mometasone furoate, micronized	15279003	1
Caecolo/Gehe	Mometasone furoate, micronized	16J24-B11-332112	1
Caesar & Loretz GmbH	Mometasone furoate, micronized	12035601	1
Caesar & Loretz GmbH	Mometasone furoate, micronized	18334101	2
Caesar & Loretz GmbH	Mometasone furoate, micronized	18026012	2
Caesar & Loretz GmbH	Mometasone furoate, micronized	18334104	3
Caesar & Loretz GmbH	Mometasone furoate, micronized	18334102	2
Caesar & Loretz GmbH	Mometasone furoate, micronized	18334108	2
Caesar & Loretz GmbH	Mometasone furoate, micronized	18334110	1
Caesar & Loretz GmbH	Mometasone furoate, micronized	19200601	2
Caesar & Loretz GmbH	Mometasone furoate, micronized	19200602	1
Caesar & Loretz GmbH, 4...	Mometasone furoate, micronized	11H10-N04	1
Caesar u Loretz	Mometasone furoate, micronized	15279004	2
caesar&Loretz GmbH,Phön...	Mometasone furoate, micronized	16028604	1
Cealo/Anzag	Mometasone furoate, micronized	18026012	1
Fagron	Mometasone furoate, micronized	15G08B11322738	1
Fagron	Mometasone furoate, micronized	15B11B03304122	1
EuRho	Mometasone furoate, micronized	1408010-01	1
EuRho	Mometasone furoate, micronized	15/11-B02-315705	1
EuRho/Phönix	Mometasone furoate, micronized	1307037-01	2
Euro OTC	Mometasone furoate, micronized	1203024-02	1
Euro OTC	Mometasone furoate, micronized	1408010-01	2
Euro OTC	Mometasone furoate, micronized	1504012-01	7
Euro OTC	Mometasone furoate, micronized	1510036-01	9
Euro OTC	Mometasone furoate, micronized	1606021-01	5
Euro OTC	Mometasone furoate, micronized	5991	1
Euro OTC	Mometasone furoate, micronized	23051822	1
Euro OTC	Mometasone furoate, micronized	17D19-B02-342643	1
Euro OTC	Mometasone furoate, micronized	1810008-01	7
Euro OTC	Mometasone furoate, micronized	18B19-B07-352632	1
Euro OTC	Mometasone furoate, micronized	181000801	1
Euro OTC	Mometasone furoate, micronized	1906035-01	5
Euro OTC	Mometasone furoate, micronized	1906035	2
Euro OTC	Mometasone furoate, micronized	1711027-01	7
Euro OTC	Mometasone furoate, micronized	1610009-01	15
Euro OTC	Mometasone furoate, micronized	1810008_01	1
Euro OTC	Mometasone furoate, micronized	1504012-02	4
Euro OTC	Mometasone furoate, micronized	15G08-B11-322738	2
Euro OTC	Mometasone furoate, micronized	16j24-B11-332111	1
Euro OTC	Mometasone furoate, micronized	160602101	1
Euro OTC	Mometasone furoate, micronized	15G08-B11-317182	1
Euro OTC	Mometasone furoate, micronized	1711027	1
Euro OTC	Mometasone furoate, micronized	1307037-01	1
Euro OTC	Mometasone furoate, micronized	1711027-02	1
Euro OTG	Mometasone furoate, micronized	1403015-01	1
Euro OTC	Mometasone furoate, micronized	17D19B02347349	1
Fagr/sana EK: EUR 39,21 /...	Mometasone furoate, micronized	18B19-B07-35151	1
Fagro	Mometasone furoate, micronized	1511B02	1
Fagro/Noweda	Mometasone furoate, micronized	17D19-B02-339277	1
Fagron	Mometasone furoate, micronized	16J24-B11-329817	4
Fagron	Mometasone furoate, micronized	17D19-B02-342643	19

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Mometasone furoate, micronized	11C02-N03	2
Fagron	Mometasone furoate, micronized	11K28-N09	2
Fagron	Mometasone furoate, micronized	12H09-N02	7
Fagron	Mometasone furoate, micronized	12J29-N03	4
Fagron	Mometasone furoate, micronized	12J29-N01	1
Fagron	Mometasone furoate, micronized	12I29-N03	1
Fagron	Mometasone furoate, micronized	11H10-N01	1
Fagron	Mometasone furoate, micronized	12B22-N04	1
Fagron	Mometasone furoate, micronized	13F7-N01	1
Fagron	Mometasone furoate, micronized	10805-N12	1
Fagron	Mometasone furoate, micronized	13f17-n01	1
Fagron	Mometasone furoate, micronized	13j23_n02	1
Fagron	Mometasone furoate, micronized	NU0698M	2
Fagron	Mometasone furoate, micronized	14C07-B05-291266	2
Fagron	Mometasone furoate, micronized	NS1513M	1
Fagron	Mometasone furoate, micronized	14E20-B04-291265	3
Fagron	Mometasone furoate, micronized	14E20-B04	4
Fagron	Mometasone furoate, micronized	14E20-B04-291267	7
Fagron	Mometasone furoate, micronized	14e20b04291265	1
Fagron	Mometasone furoate, micronized	14e20-b04-291265	1
Fagron	Mometasone furoate, micronized	14H06-B07-297240	3
Fagron	Mometasone furoate, micronized	15B11-B03-304124	2
Fagron	Mometasone furoate, micronized	15B11-B03-304121	8
Fagron	Mometasone furoate, micronized	15B11-B03	2
Fagron	Mometasone furoate, micronized	15b11-b03-308276	2
Fagron	Mometasone furoate, micronized	15b11-b03-304124	1
Fagron	Mometasone furoate, micronized	15B11-B03-308276	2
Fagron	Mometasone furoate, micronized	15G08-B11-310864	8
Fagron	Mometasone furoate, micronized	15/11-B02-315705	3
Fagron	Mometasone furoate, micronized	15/11-B02	4
Fagron	Mometasone furoate, micronized	10E31-N26	1
Fagron	Mometasone furoate, micronized	NU2504M	1
Fagron	Mometasone furoate, micronized	5/0715	1
Fagron	Mometasone furoate, micronized	15J11-B02-315705	1
Fagron	Mometasone furoate, micronized	11H10-N04	1
Fagron	Mometasone furoate, micronized	15I11-B02-315705	1
Fagron	Mometasone furoate, micronized	15B11B03308860	1
Fagron	Mometasone furoate, micronized	15/11B02315705	2
Fagron	Mometasone furoate, micronized	15B11B03304121	1
Fagron	Mometasone furoate, micronized	16A20-B06-319749	6
Fagron	Mometasone furoate, micronized	140305MF	1
Fagron	Mometasone furoate, micronized	15G08-B11-322738	3
Fagron	Mometasone furoate, micronized	15G08	1
Fagron	Mometasone furoate, micronized	15g08-b11-322738	1
Fagron	Mometasone furoate, micronized	16A20-B06-319740	1
Fagron	Mometasone furoate, micronized	16C24-B03-324851	4
Fagron	Mometasone furoate, micronized	16C24B03324852	1
Fagron	Mometasone furoate, micronized	16C24-B03-326790	9
Fagron	Mometasone furoate, micronized	16j24-b11-329817	1
Fagron	Mometasone furoate, micronized	16C24	1
Fagron	Mometasone furoate, micronized	MOM010/0116	2
Fagron	Mometasone furoate, micronized	16C24B03	1
Fagron	Mometasone furoate, micronized	16C24-B03-328272	5
Fagron	Mometasone furoate, micronized	16J24-B11-332112	11
Fagron	Mometasone furoate, micronized	6071716	1
Fagron	Mometasone furoate, micronized	16J24-B11-334371	7
Fagron	Mometasone furoate, micronized	MOM004/0716	3
Fagron	Mometasone furoate, micronized	17D19-B02339277	1
Fagron	Mometasone furoate, micronized	16j24-b11-335792	1
Fagron	Mometasone furoate, micronized	MOM001/0317	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Mometasone furoate, micronized	334371	1
Fagron	Mometasone furoate, micronized	17D19-B02-344776	2
Fagron	Mometasone furoate, micronized	347349	2
Fagron	Mometasone furoate, micronized	17D19-B02-347349	11
Fagron	Mometasone furoate, micronized	18B19-B07-341351	1
Fagron	Mometasone furoate, micronized	MOM010/0118	5
Fagron	Mometasone furoate, micronized	17d19-b02-347349	1
Fagron	Mometasone furoate, micronized	18B19-B07-352745	5
Fagron	Mometasone furoate, micronized	352632	1
Fagron	Mometasone furoate, micronized	18819-b07	1
Fagron	Mometasone furoate, micronized	18B19-B07-354318	2
Fagron	Mometasone furoate, micronized	18B19-B07-357640	5
Fagron	Mometasone furoate, micronized	19F13-B12-1917610481	1
Fagron	Mometasone furoate, micronized	19F13-B12-191761	4
Fagron	Mometasone furoate, micronized	18B19-B07-357228	1
Fagron	Mometasone furoate, micronized	19F13-B12-191762	1
Fagron	Mometasone furoate, micronized	MOM003/0818	1
Fagron	Mometasone furoate, micronized	13F27-N02	6
Fagron	Mometasone furoate, micronized	16/24-B11-332122	1
Fagron	Mometasone furoate, micronized	14H06-B07-298481	2
Fagron	Mometasone furoate, micronized	18B19-B07-351351	3
Fagron	Mometasone furoate, micronized	18B19-B07-352632	10
Fagron	Mometasone furoate, micronized	12B22-N01	1
Fagron	Mometasone furoate, micronized	NT1568M	3
Fagron	Mometasone furoate, micronized	16J24-B11	4
Fagron	Mometasone furoate, micronized	15G08-B11-0002	1
Fagron	Mometasone furoate, micronized	13j23-no2	1
Fagron	Mometasone furoate, micronized	14H06-B07297240	1
Fagron	Mometasone furoate, micronized	16J24-B11-330978	4
Fagron	Mometasone furoate, micronized	15B11-B03-308860	2
Fagron	Mometasone furoate, micronized	18B19-B07-354320	9
Fagron	Mometasone furoate, micronized	4(18B19-B07-351001	1
Fagron	Mometasone furoate, micronized	13d08-n06	1
Fagron	Mometasone furoate, micronized	14E20-B04-294645	6
Fagron	Mometasone furoate, micronized	14C07-B05-291264	1
Fagron	Mometasone furoate, micronized	14E20-B04-302374	2
Fagron	Mometasone furoate, micronized	18B19-B07-352635	1
Fagron	Mometasone furoate, micronized	18819-B07-357640	2
Fagron	Mometasone furoate, micronized	13j23-N02	1
Fagron	Mometasone furoate, micronized	16C24-B03-324852	4
Fagron	Mometasone furoate, micronized	11F08-N03	1
Fagron	Mometasone furoate, micronized	11h10-n04	1
Fagron	Mometasone furoate, micronized	18B19-B07	6
Fagron	Mometasone furoate, micronized	18B19-B07-354319	2
Fagron	Mometasone furoate, micronized	13D08N06	1
Fagron	Mometasone furoate, micronized	15/11-B02-314479	5
Fagron	Mometasone furoate, micronized	14e20-b04-291267	1
Fagron	Mometasone furoate, micronized	16A20-B06	3
Fagron	Mometasone furoate, micronized	17D19-B02	1
Fagron	Mometasone furoate, micronized	13F27-N02	1
Fagron	Mometasone furoate, micronized	16A20-B06319749	1
Fagron	Mometasone furoate, micronized	13D08-N06	14
Fagron	Mometasone furoate, micronized	15G08-B11	2
Fagron	Mometasone furoate, micronized	701834-0004	1
Fagron	Mometasone furoate, micronized	14E20-B04-291269	2
Fagron	Mometasone furoate, micronized	16J24B11332112	1
Fagron	Mometasone furoate, micronized	13H13-N04	1
Fagron	Mometasone furoate, micronized	14C07-B05-291268	5
Fagron	Mometasone furoate, micronized	16C24B03324851	1
Fagron	Mometasone furoate, micronized	16J24-B11-335793	10

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Mometasone furoate, micronized	17D19B02342642	1
Fagron	Mometasone furoate, micronized	18B19B07352745	1
Fagron	Mometasone furoate, micronized	16C24-B03-327346	4
Fagron	Mometasone furoate, micronized	16A20-B06-322739	4
Fagron	Mometasone furoate, micronized	16c24-b03-327372	1
Fagron	Mometasone furoate, micronized	15B11-B03-304122	6
Fagron	Mometasone furoate, micronized	16A20-B06-319748	6
Fagron	Mometasone furoate, micronized	16J24-B11-332110	1
Fagron	Mometasone furoate, micronized	17D19_B02_339278	1
Fagron	Mometasone furoate, micronized	16C24-B03-327372	5
Fagron	Mometasone furoate, micronized	1814E3640	1
Fagron	Mometasone furoate, micronized	2114M3640	1
Fagron	Mometasone furoate, micronized	MOM008/0915	3
Fagron	Mometasone furoate, micronized	16C24-B03	2
Fagron	Mometasone furoate, micronized	16181714	1
Fagron	Mometasone furoate, micronized	16j24-b11	1
Fagron	Mometasone furoate, micronized	16J24B11334371	1
Fagron	Mometasone furoate, micronized	335793	1
Fagron	Mometasone furoate, micronized	18B19-B07-352744	2
Fagron	Mometasone furoate, micronized	10C29-N10	1
Fagron	Mometasone furoate, micronized	3313A-07030	1
Fagron	Mometasone furoate, micronized	2714U-07030	1
Fagron	Mometasone furoate, micronized	14H06-B07-302375	2
Fagron	Mometasone furoate, micronized	2215I-07030	1
Fagron	Mometasone furoate, micronized	13Do8-N06	1
Fagron	Mometasone furoate, micronized	15G08-B11-322737	2
Fagron	Mometasone furoate, micronized	17D19-B02-339278	3
Fagron	Mometasone furoate, micronized	17D19-B02-347348	3
Fagron	Mometasone furoate, micronized	18B19-B07-351001	1
Fagron	Mometasone furoate, micronized	16724-B11-332112	1
Fagron	Mometasone furoate, micronized	15B11-B03-304120	7
Fagron	Mometasone furoate, micronized	12e02-n11	1
Fagron	Mometasone furoate, micronized	15G-B11-310864	1
Fagron	Mometasone furoate, micronized	15/11-B02-316705	1
Fagron	Mometasone furoate, micronized	16C24-b03-327372	1
Fargon	Mometasone furoate, micronized	13H13-N04	1
Fargon	Mometasone furoate, micronized	14h06-b07-298481	1
Fargon	Mometasone furoate, micronized	16C24-B03-324852	1
Finteler Apotheke	Mometasone furoate, micronized	16028604	1
Finteler Apotheke	Mometasone furoate, micronized	16028603	1
Fragon/Sanacorp	Mometasone furoate, micronized	16C24-B03-324851	1
Fragon/Sanacorp	Mometasone furoate, micronized	17D19-B02-339277	2
Fragon/Sanacorp	Mometasone furoate, micronized	17D19-B02-342642	1
Fragon/Sanacorp	Mometasone furoate, micronized	17D19-B02-347348	1
Fragon/Sanacorp	Mometasone furoate, micronized	17D19-B02-342643	2
Gehe	Mometasone furoate, micronized	13D08-N06	1
Gehe	Mometasone furoate, micronized	13H13-N04	2
Gehe	Mometasone furoate, micronized	16353201	1
Gehe	Mometasone furoate, micronized	16353207	1
Gehe	Mometasone furoate, micronized	18334101	1
Gehe	Mometasone furoate, micronized	1906035-01	3
GEHE	Mometasone furoate, micronized	18026006	1
Gehe 07.12.18	Mometasone furoate, micronized	1711027_02	1
GEHE 17.04.2014	Mometasone furoate, micronized	13J23-N02	1
Fagron	Mometasone furoate, micronized	16J24-B11-332111	2
Fagron	Mometasone furoate, micronized	16J24-11-335793	1
Holdermann	Mometasone furoate, micronized	13D08-N06	1
Holdermann	Mometasone furoate, micronized	14C07-B05-29126	1
Ichthyol-Gesellschaft/Ph. ...	Mometasone furoate, micronized	16J24-B11-335793	2
Jenne	Mometasone furoate, micronized	18026012	1

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Supplier	Substance	Batch	Spectra
Jenne	Mometasone furoate, micronized	1802612	1
Kehr	Mometasone furoate, micronized	16353206	1
Fagron	Mometasone furoate, micronized	16J24-B11-335792	1
Fagron	Mometasone furoate, micronized	16C24-803-324851	1
Fagron	Mometasone furoate, micronized	17D19-B02-339277	3
Noveda	Mometasone furoate, micronized	18334101	1
Noweda	Mometasone furoate, micronized	16C24-B03-328272	1
Noweda	Mometasone furoate, micronized	16J24-B11-332111	1
Noweda	Mometasone furoate, micronized	18026009	1
Noweda	Mometasone furoate, micronized	15G08-B11	1
Noweda	Mometasone furoate, micronized	18334110	1
Caelo	Mometasone furoate, micronized	13304605	4
Caelo	Mometasone furoate, micronized	14281103	2
Caelo	Mometasone furoate, micronized	15110301	2
Euro OTC	Mometasone furoate, micronized	161000901	1
Fagron	Mometasone furoate, micronized	12E02-N11	3
Fagron	Mometasone furoate, micronized	13H13-N04	10
Fagron	Mometasone furoate, micronized	13J23-N02	20
Fagron	Mometasone furoate, micronized	14H06-B07-298482	7
Fagron	Mometasone furoate, micronized	14H06-B07-302376	2
Fagron	Mometasone furoate, micronized	15B11-B03-304123	13
Phagron	Mometasone furoate, micronized	19F13-B12-191761	1
phoenix	Mometasone furoate, micronized	18334108	1
Phoenix	Mometasone furoate, micronized	14C07-B05-291268	1
Phoenix	Mometasone furoate, micronized	16181714	1
Phoenix	Mometasone furoate, micronized	MOM004/0716	1
Phoenix	Mometasone furoate, micronized	17D19-B02-339277	1
Phoenix	Mometasone furoate, micronized	18B19-B07-352745	1
Phoenix	Mometasone furoate, micronized	1810008-01	1
Phoenix	Mometasone furoate, micronized	3406	1
Caelo	Mometasone furoate, micronized	16181708	4
phönix	Mometasone furoate, micronized	15B11-b03	1
Phönix	Mometasone furoate, micronized	13D08-N06	1
Phönix	Mometasone furoate, micronized	13/23-N02	2
Phönix	Mometasone furoate, micronized	14E20-B04-291267	1
Phönix	Mometasone furoate, micronized	15G08-B11-322737	1
Phönix	Mometasone furoate, micronized	16c24-b03-327346	1
Phönix	Mometasone furoate, micronized	17D19-B02-342642	1
Phönix	Mometasone furoate, micronized	18026012	1
Caelo	Mometasone furoate, micronized	17D19-B02-34476	1
Phönix Gotha	Mometasone furoate, micronized	1403015-01	1
Sana	Mometasone furoate, micronized	MF-18009(JM-01)001	1
Sanacorp	Mometasone furoate, micronized	14E20-B04-291267	1
Sanacorp	Mometasone furoate, micronized	1/AKD4	1
Sanacorp	Mometasone furoate, micronized	15189801	1
Sanacorp	Mometasone furoate, micronized	16353211	1
Sanacorp	Mometasone furoate, micronized	17D19-B02-339276	1
Sanacorp	Mometasone furoate, micronized	17D19-B02-344776	2
Sanacorp	Mometasone furoate, micronized	MOM001/0317	1
Sanacorp	Mometasone furoate, micronized	18026001	1
Caelo	Mometasone furoate, micronized	12035601	1
SanacorpWE:12.01.2017 ...	Mometasone furoate, micronized	16028602	1
sidonia	Mometasone furoate, micronized	18334110	1
Caelo	Mometasone furoate, micronized		1
Caesar&loretz,AHC,08.08...	Mometasone furoate, micronized		1
Fagron	Mometasone furoate, micronized	13F17-N01	8
Fagron	Mometasone furoate, micronized		1

- 110 172 spectra from 742 *Apo-Ident* customers from a total of 31 575 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mometasone furoate, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mometasone furoate, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	475	0	110 214
Type B	0	436	60	118 646
Type C	0	963	112	110 172

The substance/substance group *Mometasone furoate, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.7368 %)
Type B	100.0000 % (> 99.9893 %)	87.9032 % (> 87.2984 %)
Type C	100.0000 % (> 99.8899 %)	89.5814 % (> 89.3023 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mometasone furoate, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Atropine sulfate	62.49	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mometasone furoate, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20850	22433	2.51	68.87
22433	22433	0.00	69.74
23046	23046	0.00	69.29
22887	22238	3.87	70.49
23136	23136	0.00	70.33
22238	22238	0.00	71.73
21602	22433	4.73	71.57

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Monostereates**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20691-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Monostereates; Glycerol monostearate 40-55%; Glycerol monostearate 60; Glycerol monostearate, emulsifying; Glyceroli monostearates 40-55%; Glyceroli monostearates 60; Glyceroli monostearates emulsificantes; Softisan[®] 601; Sorbitan stearate; Sorbitani stearas

Special notes

When selecting the *Monostereates* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Glycerol monostearate 40-55%	6	3	23
Glycerol monostearate 60	7	2	16
Glycerol monostearate, emulsifying	4	5	15
Softisan [®] 601	3	2	3
Sorbitan stearate	6	5	30

Second-stage model

For differentiation of the substance/substance group *Monostereates* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Monostereates*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Glycerol monoste...	12105705	20691	80	20120424
Caelo	Glycerol monoste...	12105720	20867	40	20120424
Caelo	Glycerol monoste...	14099903	21446	60	AR-15-FG-000732-02
Caelo	Glycerol monoste...	154450	22464	60	20160225*
Fagron	Glycerol monoste...	14C12-B40-292622	21545	60	20140404
Fagron	Glycerol monoste...	15E13-B03-305532	22277	60	20150703
Caelo	Glycerol monoste...	13109304	21093	40	1407633
Caelo	Glycerol monoste...	13232604	21437	60	1504599
Caelo	Glycerol monoste...	15286302	21982	60	20150911
Caelo	Glycerol monoste...	15286302	22320	60	AR-16-FG-009226-01
Caelo	Glycerol monoste...	16233804	23188	40	10052
Caelo	Glycerol monoste...	180683	24025	40	20180430*
Caelo	Glycerol monoste...	182462	24371	40	20181008*
Caelo	Glycerol monoste...	190547	24673	40	20190423*
Caelo	Glycerol monoste...	12210401	20751	80	1407214
Caelo	Glycerol monoste...	12210401	20783	40	20120726
Caelo	Glycerol monoste...	14240607	21576	60	1412120
Caelo	Glycerol monoste...	14240607	21585	60	20140815
Caelo	Glycerol monoste...	161646	22623	40	20160727*
Caelo	Glycerol monoste...	16030301	22667	40	20160204
Caelo	Softisan® 601	13296104	20997	40	1403144
Caelo	Softisan® 601	15184905	21974	60	20150611
Caelo	Softisan® 601	172178	23690	40	20170817*
Caelo	Sorbitan stearate	12274801	20828	40	20120924
Caelo	Sorbitan stearate	162352	22764	40	20160826*
Caelo	Sorbitan stearate	17030805	23706	40	20170210
Caelo	Sorbitan stearate	172564	23831	40	20171027*
Caelo	Sorbitan stearate	192928	25094	40	20191122*
Fagron	Sorbitan stearate	14J07-B02-299399	21885	60	AR-16-FG-004368-01

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1460 spectra of 29 reference samples from the substance/substance group *Monostereates*. These

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

samples are listed above in the [calibration samples](#) section. The reference samples come from 26 different batches.

- 109 229 spectra from a total of 1940 batches from further 386 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1100 spectra of 24 reference samples from the substance/substance group *Monostereates*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Glycerol monostearate 40-55%	180447	24267	40
Caelo	Glycerol monostearate 40-55%	190794	24709	40
Caelo	Glycerol monostearate 40-55%	191186	24713	40
Caelo	Glycerol monostearate 60	11272902	20677	80
Caelo	Glycerol monostearate 60	162338	22646	40
Caelo	Glycerol monostearate, emuls. ...	11079309	20621	40
Caelo	Glycerol monostearate, emuls. ...	14308310	21993	60
Caelo	Glycerol monostearate, emuls. ...	172585	23822	40
Fagron	Glycerol monostearate, emuls. ...	11I15-N09	20746	80
Fagron	Glycerol monostearate, emuls. ...	12B14-N10	20786	40
Caelo	Softisan® 601	14099604	21488	40
Caelo	Softisan® 601	162364	22648	40
Caelo	Sorbitan stearate	171781	23622	40
Caelo	Sorbitan stearate	180432	24021	40
Caelo	Sorbitan stearate	183125	24377	40
Caelo	Sorbitan stearate	192168	24900	40
Fagron	Sorbitan stearate	11I26-N09	20736	40
Caelo	Glycerol monostearate 60	162338	22741	40
Caelo	Glycerol monostearate 60	162338	22742	40
Caelo	Glycerol monostearate 60	162338	22743	40
Caelo	Glycerol monostearate 60	162338	22744	40
Caelo	Glycerol monostearate, emuls. ...	14308310	22278	60
Caelo	Glycerol monostearate, emuls. ...	14308310	22341	60
Caelo	Softisan® 601	162364	22766	40

- 118 042 spectra from a total of 2403 batches from further 795 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples

are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 245 spectra from 125 *Apo-Ident* customers from 97 batches from the substance/substance group *Monostereates*.
- Among them are spectra of independent samples from 86 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Glycerol monostearate 40-55%	12105704	1
Caelo	Glycerol monostearate 40-55%	131156602	1
Caelo	Glycerol monostearate 40-55%	13221308	1
Caelo	Glycerol monostearate 40-55%	14169710	1
Caelo	Glycerol monostearate 40-55%	15280912	1
Caelo	Glycerol monostearate 40-55%	14359407	1
Caelo	Glycerol monostearate 40-55%	15445007	5
Caelo	Glycerol monostearate 40-55%	15445010	1
Caelo	Glycerol monostearate 40-55%	18044702	1
Caelo	Glycerol monostearate 40-55%	13221303	2
Caelo	Glycerol monostearate 40-55%	18044701	2
Caelo	Glycerol monostearate 40-55%	15445011	1
Caelo	Glycerol monostearate 40-55%	15280904	2
Caelo	Glycerol monostearate 40-55%	19079401	1
Caelo	Glycerol monostearate 40-55%	15445014	1
Caelo	Glycerol monostearate 40-55%	15280903	2
Caelo	Glycerol monostearate 40-55%	12105729	1
Caesar/Noweda	Glycerol monostearate 40-55%	13221311	2
Fagron	Glycerol monostearate 40-55%	12A27-N11	1
Fagron	Glycerol monostearate 40-55%	12K05-N06	1
Fagron	Glycerol monostearate 40-55%	15280903	1
Fagron	Glycerol monostearate 40-55%	7G19-N09	1
Spangropharm	Glycerol monostearate 40-55%	80402468	1
Caelo	Glycerol monostearate 40-55%	13156601	2
Anzag	Glycerol monostearate 60	12180502	1
Audor Pharma	Glycerol monostearate 60	13232604	1
Caelo	Glycerol monostearate 60	13018201	3
Caelo	Glycerol monostearate 60	1301821	1
Caelo	Glycerol monostearate 60	17061703	3
Caelo	Glycerol monostearate 60	19054702	5
Caelo	Glycerol monostearate 60	18068303	2
Caelo	Glycerol monostearate 60	16233802	1
Caelo	Glycerol monostearate 60	15009203	13
Caelo	Glycerol monostearate 60	15286308	4
Caelo	Glycerol monostearate 60	15286307	2
Caelo	Glycerol monostearate 60	17167804	5
Caelo	Glycerol monostearate 60	18246207	1
Caelo	Glycerol monostearate 60	14012002	4
Caesar & Loretz/Noweda	Glycerol monostearate 60	15009203	1
Caesar u Loretz	Glycerol monostearate 60	13109304	1
Caesar u Loretz	Glycerol monostearate 60	14012002	1
Caesar/Noweda	Glycerol monostearate 60	13109304	1
Euro OTC	Glycerol monostearate 60	16233804	1
Fagron	Glycerol monostearate 60	15009203	1
Gehe	Glycerol monostearate 60	19054702	1
Caelo	Glycerol monostearate 60	17167803	5
L12	Glycerol monostearate 60	16233802	2
Noweda	Glycerol monostearate 60	15009203	1

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Supplier	Substance	Batch	Spectra
Phonix	Glycerol monostearate 60	13109304	1
Caelo	Glycerol monostearate 60	12001001	1
Caelo	Glycerol monostearate, emuls...	18328702	2
Caelo	Glycerol monostearate, emuls...	11079308	1
Caelo	Glycerol monostearate, emuls...	13109405	2
Caelo	Glycerol monostearate, emuls...	13109402	1
Caelo	Glycerol monostearate, emuls...	14240611	1
Caelo	Glycerol monostearate, emuls...	14308310	4
Caelo	Glycerol monostearate, emuls...	16030304	2
Caelo	Glycerol monostearate, emuls...	16164604	1
Caelo	Glycerol monostearate, emuls...	16164606	1
Caelo	Glycerol monostearate, emuls...	13109410	1
Caelo	Glycerol monostearate, emuls...	1420607	1
Caelo	Glycerol monostearate, emuls...	17258501	1
Gehe	Glycerol monostearate, emuls...	14240605	2
Gehe	Glycerol monostearate, emuls...	18328702	1
Caelo	Glycerol monostearate, emuls...	17258505	2
Noweda	Glycerol monostearate, emuls...	11079301	1
Caelo	Softisan® 601	15184901	1
Caelo	Softisan® 601	14099608	1
Caesar & Loretz GmbH	Softisan® 601	18197002	1
ALH	Sorbitan stearate	16235202	1
anzag	Sorbitan stearate	14195	1
Caelo	Sorbitan stearate	12274807	1
Caelo	Sorbitan stearate	13209410	1
Caelo	Sorbitan stearate	13209409	2
Caelo	Sorbitan stearate	14038510	1
Caelo	Sorbitan stearate	14218803	3
Caelo	Sorbitan stearate	14218808	3
Caelo	Sorbitan stearate	26031507	1
Caelo	Sorbitan stearate	16235207	10
Caelo	Sorbitan stearate	17030806	1
Caelo	Sorbitan stearate	17345402	2
Caelo	Sorbitan stearate	14218804	1
Caelo	Sorbitan stearate	13B19-N01	1
Caelo	Sorbitan stearate	15300302	7
Caelo	Sorbitan stearate	14038504	1
Caelo	Sorbitan stearate	13209417	3
Caelo	Sorbitan stearate	14038511	2
Caelo	Sorbitan stearate	15415202	8
Caelo	Sorbitan stearate	13209419	3
Caelo	Sorbitan stearate	12274813	2
Caelo	Sorbitan stearate	15300308	4
Caelo	Sorbitan stearate	13209418	2
Caelo	Sorbitan stearate	13209409	1
Fagron	Sorbitan stearate	5052	1
Fagron	Sorbitan stearate	12E30-N14	1
Fagron	Sorbitan stearate	13B19-N01	1
Fagron	Sorbitan stearate	13D10_N10	1
Fagron	Sorbitan stearate	13D10-N10	1
Ichthyol/Phoenix	Sorbitan stearate	14372803	1
Caelo	Sorbitan stearate	18204705	2
Caelo	Sorbitan stearate	14372803	1
Caelo	Sorbitan stearate	16235202	3
Phonix	Sorbitan stearate	13209418	1
Caelo	Sorbitan stearate	17178102	13
Caelo	Glycerol monostearate 60	13109304	9
Caelo	Glycerol monostearate 60	13232604	3
Caelo	Glycerol monostearate 60	15286302	3
Caelo	Glycerol monostearate 60	16233804	5

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Supplier	Substance	Batch	Spectra
Caelo	Glycerol monostearate 60		1
Caelo	Glycerol monostearate, emuls. ...	14240607	1
Caelo	Glycerol monostearate, emuls. ...	16030301	3
Caelo	Softisan® 601	13296104	1
Caelo	Sorbitan stearate	17030805	5
Fagron	Sorbitan stearate	14J07-B02-299399	1
Nachprüfung	Sorbitan stearate		1

- 111 002 spectra from 742 *Apo-Ident* customers from a total of 31 796 batches from a further 702 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Monostereates* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Monostereates* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	1460	0	109 229
Type B	0	923	177	118 042
Type C	0	232	13	111 002

The substance/substance group *Monostereates* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.5890 %)
Type B	100.0000 % (> 99.9893 %)	83.9091 % (> 83.6364 %)
Type C	100.0000 % (> 99.8899 %)	94.6939 % (> 93.4694 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Monostereates* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Wool alcohols	20.59	—
Menthol	29.55	—
Emulsifying cetostearyl alcohol (type A)	30.32	—
Cetomacrogol emulsifying wax 1000 NI	35.60	—
Cetostearyl alcohol	39.81	—
Magnesium stearate	41.11	—
Biotin	41.85	—
Cetyl alcohol	46.83	—
Non-ionic emulsifying alcohol	49.92	—
Ascorbyl palmitate	51.83	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Monostereates* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22623	22623	0.00	43.67
23690	23690	0.00	39.91
22277	21446	19.45	33.47
22464	22464	0.00	32.81
20751	20751	0.00	35.11
20783	20751	2.53	35.10
22667	20751	8.15	31.41
21974	20997	11.20	42.41
21885	21885	0.00	45.73
24673	24673	0.00	41.12
24025	24025	0.00	41.57
22764	22764	0.00	43.70
23706	22764	3.46	43.52
23831	23831	0.00	47.66
25094	25094	0.00	44.04
21982	22320	2.79	35.60
22320	22320	0.00	36.71
24371	24371	0.00	37.17
20997	20997	0.00	41.48
21093	21093	0.00	43.30
21576	21576	0.00	40.02
21585	21576	1.62	39.67
21437	21437	0.00	34.53
23188	23188	0.00	36.94
20828	25094	19.43	39.13
20691	21446	6.84	39.77
20867	21446	17.96	40.76
21446	21446	0.00	37.34
21545	21446	13.74	40.74

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Mupirocin calcium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20781-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Mupirocin calcium; Mupirocinum calcii

Special notes

When selecting the *Mupirocin calcium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Mupirocin calcium	4	1	11

Second-stage model

For differentiation of the substance/substance group *Mupirocin calcium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Mupirocin calcium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Mupirocin calcium	14276602	21745	60	20141103
Caelo	Mupirocin calcium	161184	22454	60	20160504*
Fagron	Mupirocin calcium	12E02-N07	20781	40	1401556
Fagron	Mupirocin calcium	15H13-B01-316111	23213	40	20150909

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Mupirocin calcium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 489 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Mupirocin calcium*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Mupirocin calcium	161608	23860	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 8 *Apo-Ident* customers from 11 batches from the substance/substance group *Mupirocin calcium*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Mupirocin calcium	9041801	1
Caelo	Mupirocin calcium	17356502	1
Caelo	Mupirocin calcium	24041801	1
Caelo	Mupirocin calcium	17356506	1
Caelo	Mupirocin calcium	83200301013	1
Caelo	Mupirocin calcium	18191601	1
Fagron	Mupirocin calcium	14B03-B30-297291	1
Fagron	Mupirocin calcium	17F21-B03-338597	1
Fagron	Mupirocin calcium	17F21-B03-339080	1
Fagron	Mupirocin calcium	83200340116	1
Fagron	Mupirocin calcium	15H13-B01	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Mupirocin calcium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mupirocin calcium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	40	0	119 102
Type C	0	11	0	111 236

The substance/substance group *Mupirocin calcium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Mupirocin calcium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Soy lecithin (instant form)	49.27	—
Menthol	54.13	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Mupirocin calcium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20781	20781	0.00	45.37
21745	22454	4.71	46.22
22454	22454	0.00	47.76
23213	22454	8.16	46.81

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Naloxone hydrochloride dihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20957-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Naloxone hydrochloride dihydrate; Naloxoni hydrochloridum dihydricum

Special notes

When selecting the *Naloxone hydrochloride dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Naloxone hydrochloride dihydrate	6	3	21

Second-stage model

For differentiation of the substance/substance group *Naloxone hydrochloride dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Naloxone hydrochloride dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Naloxone hydroch...	AP13501078IIN	22811	40	20160429
Audor Pharma	Naloxone hydroch...	AP1547I022-1N	24707	40	20180629
Caelo	Naloxone hydroch...	163577	23039	40	20170306*
Caelo	Naloxone hydroch...	170441	23862	40	20170306*
Fagron	Naloxone hydroch...	13D22-N07	20957	40	1402059
Fagron	Naloxone hydroch...	13L12-B03	21271	40	20140113

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Naloxone hydrochloride dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 449 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Naloxone hydrochloride dihydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Naloxone hydrochloride dihyd...	15322517	22828	40
Caelo	Naloxone hydrochloride dihyd...	190088	24537	40
Euro OTC	Naloxone hydrochloride dihyd...	2002011	25134	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 36 spectra from 9 *Apo-Ident* customers from 21 batches from the substance/substance group *Naloxone hydrochloride dihydrate*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Naloxone hydrochloride dihyd...	AP13501078N	1
Caelo	Naloxone hydrochloride dihyd...	18134202	1
Caesar & Loretz GmbH	Naloxone hydrochloride dihyd...	19008803	1
Fagron	Naloxone hydrochloride dihyd...	11/23-N01	1
Fagron	Naloxone hydrochloride dihyd...	12G19-N02	2
Fagron	Naloxone hydrochloride dihyd...	12-00071	2
Fagron	Naloxone hydrochloride dihyd...	12G19-N02	1
Fagron	Naloxone hydrochloride dihyd...	14A28-B33-296076	1
Fagron	Naloxone hydrochloride dihyd...	15B06-B02-304421	1
Fagron	Naloxone hydrochloride dihyd...	15H04-B09-314068	4
Fagron	Naloxone hydrochloride dihyd...	14F20-B02-296077	1
Fagron	Naloxone hydrochloride dihyd...	13L12-B03-289511	1
Fagron	Naloxone hydrochloride dihyd...	18K20-B05-356947	1
Fagron	Naloxone hydrochloride dihyd...	15E28-B01-308324	5
Fagron	Naloxone hydrochloride dihyd...	18K20-B05-356948	1
Fagron	Naloxone hydrochloride dihyd...	15H04-B09	3
Fagron	Naloxone hydrochloride dihyd...	13-00660	1
Fagron	Naloxone hydrochloride dihyd...	15B06-B02-304420	2
Fagron	Naloxone hydrochloride dihyd...	1350I078	1
Fagron	Naloxone hydrochloride dihyd...	15K11-B05-319571	4
Fagron	Naloxone hydrochloride dihyd...	15K11-B05_319571	1

- 111 211 spectra from 742 *Apo-Ident* customers from a total of 31 870 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Naloxone hydrochloride dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Naloxone hydrochloride dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	120	0	119 022
Type C	0	34	2	111 211

The substance/substance group *Naloxone hydrochloride dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	94.4444 % (> 86.1111 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Naloxone hydrochloride dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxycodone hydrochloride	37.30	—
Estriol	41.57	—
Sildenafil citrate	46.20	—
Oxybutynin hydrochloride	53.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Naloxone hydrochloride dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24707	23039	18.07	50.92
22811	23039	8.35	46.49
20957	20957	0.00	44.29
21271	20957	5.58	41.57
23862	23862	0.00	46.95
23039	23039	0.00	48.31

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Naphazoline hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20899-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Naphazoline hydrochloride; Naphazolini hydrochloridum

Special notes

When selecting the *Naphazoline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Naphazoline hydrochloride	4	4	83

Second-stage model

For differentiation of the substance/substance group *Naphazoline hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Naphazoline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Naphazoline hydr...	12375211	20899	40	20130108
Caelo	Naphazoline hydr...	12375211	21397	60	20130108
Caelo	Naphazoline hydr...	12375211	21398	60	20130108
Caelo	Naphazoline hydr...	181193	24498	40	20180504*
Euro OTC	Naphazoline hydr...	1407034-01	21623	60	AR-15-FG-007847-01
Euro OTC	Naphazoline hydr...	1506015	21859	60	20150727*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Naphazoline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 369 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Naphazoline hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Naphazoline hydrochloride	161741	24496	40
Euro OTC	Naphazoline hydrochloride	1607041	22753	40
Euro OTC	Naphazoline hydrochloride	1704005	23385	40
Euro OTC	Naphazoline hydrochloride	1903006	24613	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 172 spectra from 132 *Apo-Ident* customers from 87 batches from the substance/substance group *Naphazoline hydrochloride*.
- Among them are spectra of independent samples from 83 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Naphazoline hydrochloride	14070034-01	1
Caelo	Naphazoline hydrochloride	2275310	1
Caelo	Naphazoline hydrochloride	9285103	2
Caelo	Naphazoline hydrochloride	11081107	2
Caelo	Naphazoline hydrochloride	15071404	1
Caelo	Naphazoline hydrochloride	1307020-02	1
Caelo	Naphazoline hydrochloride	15223303	1
Caelo	Naphazoline hydrochloride	12176203	2
Caelo	Naphazoline hydrochloride	140703402	1
Caelo	Naphazoline hydrochloride	17C02-B05-341579	1
Caelo	Naphazoline hydrochloride	1607041-01	1
Caelo	Naphazoline hydrochloride	18D09-B08-350950	1
Caelo	Naphazoline hydrochloride	18119302	1
Caelo	Naphazoline hydrochloride	18D09-B08-352462	1
Caelo	Naphazoline hydrochloride	16174101	3
Caelo	Naphazoline hydrochloride	732570001	1
Caelo	Naphazoline hydrochloride	15223301	2
Caelo	Naphazoline hydrochloride	1506015-2	1
Caelo	Naphazoline hydrochloride	15J05-B05/171025NHC	1
Caelo	Naphazoline hydrochloride	1206037	1
Caesar & Loretz/Engel	Naphazoline hydrochloride	18119302	2
Caleo /Herba	Naphazoline hydrochloride	9285103	1
EuRho	Naphazoline hydrochloride	1114I-001885	1
Eurho/Phoenix	Naphazoline hydrochloride	4413I-01885	1
EuRho/Phönix	Naphazoline hydrochloride	1704005-03	1
Euro OTC	Naphazoline hydrochloride	1206037-01	1
Euro OTC	Naphazoline hydrochloride	1506015-02	7
Euro OTC	Naphazoline hydrochloride	616620001	1
Euro OTC	Naphazoline hydrochloride	1407034-03	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Naphazoline hydrochloride	1704005-03	1
Euro OTC	Naphazoline hydrochloride	1407034-02	4
Euro OTC	Naphazoline hydrochloride	1607041	1
Euro OTC	Naphazoline hydrochloride	1206037-02	4
Euro OTC	Naphazoline hydrochloride	1307020-03	2
Euro OTC	Naphazoline hydrochloride	1103031-02	1
Euro OTC	Naphazoline hydrochloride	150601502	1
Euro OTC	Naphazoline hydrochloride	1506015-01	2
Euro OTC	Naphazoline hydrochloride	113031-01	1
Euro OTC	Naphazoline hydrochloride	1607041-01	5
Euro OTC	Naphazoline hydrochloride	1903006-01	1
Fagron	Naphazoline hydrochloride	11J13-N08	1
Fagron	Naphazoline hydrochloride	4309I-01885	1
Fagron	Naphazoline hydrochloride	12K29-N01o256/310	1
Fagron	Naphazoline hydrochloride	13A07-N06	4
Fagron	Naphazoline hydrochloride	13C11N07	1
Fagron	Naphazoline hydrochloride	13K27-N04	12
Fagron	Naphazoline hydrochloride	13103-B03-295105	3
Fagron	Naphazoline hydrochloride	13I03-B03	2
Fagron	Naphazoline hydrochloride	13/03-B03-305291	1
Fagron	Naphazoline hydrochloride	15J05-B05-326850	3
Fagron	Naphazoline hydrochloride	15J05-B05-330834	3
Fagron	Naphazoline hydrochloride	17C02-B05-335313	5
Fagron	Naphazoline hydrochloride	17C02-B05-335113	1
Fagron	Naphazoline hydrochloride	17C02-B05-343566	4
Fagron	Naphazoline hydrochloride	18D09-B08-354882	1
Fagron	Naphazoline hydrochloride	13103-803-305291	1
Fagron	Naphazoline hydrochloride	17c02-b05-335313	1
Fagron	Naphazoline hydrochloride	1802201903	1
Fagron	Naphazoline hydrochloride	18D09-B08-350950	2
Fagron	Naphazoline hydrochloride	17C02-B05-332933	4
Fagron	Naphazoline hydrochloride	17C02-B05	3
Fagron	Naphazoline hydrochloride	13I03-B03-305291	2
Fagron	Naphazoline hydrochloride	11/05-N02	1
Fagron	Naphazoline hydrochloride	15J05-B05-322527	3
Fagron	Naphazoline hydrochloride	11K25-N03	2
Fagron	Naphazoline hydrochloride	13C11-N07	1
Fagron	Naphazoline hydrochloride	13I03-B03-295105	2
Fagron	Naphazoline hydrochloride	13/03-B03305291	1
Fagron	Naphazoline hydrochloride	17C02-B05-341579	3
Fagron	Naphazoline hydrochloride	706230001	1
Fagron	Naphazoline hydrochloride	13C11-N07	5
Fagron	Naphazoline hydrochloride	11I05-N02	2
Fagron	Naphazoline hydrochloride	17C02-B05-346657	1
Fagron	Naphazoline hydrochloride	18D09B08352462	1
Fagron	Naphazoline hydrochloride	4509E-01885	2
Fagron	Naphazoline hydrochloride	13/03-B03	1
Fagron	Naphazoline hydrochloride	15J05-B05	2
Fagron	Naphazoline hydrochloride	60494000113K27-N04	1
Fagron	Naphazoline hydrochloride	7001260012	1
Fagron	Naphazoline hydrochloride	15J05B05326850	1
Fagron	Naphazoline hydrochloride	19D03-B02-362717	1
Fagron	Naphazoline hydrochloride	13k27-n04	1
Fagron	Naphazoline hydrochloride	1303-B03	1
Fagron	Naphazoline hydrochloride	13/03-B03-295105	1
Fargon/Apo.am Park	Naphazoline hydrochloride	539580002	1
Fargon/Noweda	Naphazoline hydrochloride	17C02-B05-346657	1
Fragon GmbH/ Noweda	Naphazoline hydrochloride	15J05-B05-326850	1
Gatt-Koller	Naphazoline hydrochloride	1803834	1
Gehe/EuRo	Naphazoline hydrochloride	1607041-01	1

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Supplier	Substance	Batch	Spectra
Noweda-Fragon	Naphazoline hydrochloride	1303B03305291	1
Caelo	Naphazoline hydrochloride	1216203	1
Phonix	Naphazoline hydrochloride	1704005-02	1
Phönix	Naphazoline hydrochloride	586550002	1
Fagron	Naphazoline hydrochloride	13/03-B03-295105	2
Caelo	Naphazoline hydrochloride	12375203	1
Euro OTC	Naphazoline hydrochloride	1407034-01	2
Caelo	Naphazoline hydrochloride	12375211	1

- 111 075 spectra from 742 *Apo-Ident* customers from a total of 31 804 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Naphazoline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Naphazoline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	160	0	118 982
Type C	0	171	1	111 075

The substance/substance group *Naphazoline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	99.4186 % (> 97.6744 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Naphazoline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Diltiazem hydrochloride	25.30	—
Doxylamine hydrogen succinate	27.29	—
Omeprazole	31.67	—
L-proline	36.75	—
Dexamphetamine sulfate	38.23	—
Glycine	40.04	—
Cocaine hydrochloride	41.31	—
Ethyl hydrogen fumarate calcium	46.15	—
Diphenhydramine hydrochloride	47.31	—
Methadone hydrochloride	49.72	—
Griseofulvin	51.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Naphazoline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20899	21859	8.58	32.99
21397	21859	2.91	36.75
21398	21859	2.30	34.52
21623	21623	0.00	37.10
21859	21859	0.00	38.40
24498	24498	0.00	35.74

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Naphazoline nitrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20501-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Naphazoline nitrate; Naphazolini nitras

Special notes

When selecting the *Naphazoline nitrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Naphazoline nitrate	5	2	13

Second-stage model

For differentiation of the substance/substance group *Naphazoline nitrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Naphazoline nitrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Naphazoline nitr...	1512033	22302	60	20160126*
Euro OTC	Naphazoline nitr...	1810016	24341	40	20181112*
Euro OTC	Naphazoline nitr...	1910029	24940	40	20191125*
Fagron	Naphazoline nitr...	12L10-N03	20846	40	20121217
Fagron	Naphazoline nitr...	12J08-B40-287904	21808	60	20131129

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Naphazoline nitrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Naphazoline nitrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Naphazoline nitrate	1512033-01	23275	40
Fagron	Naphazoline nitrate	16A14-B03-327343	23164	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 13 *Apo-Ident* customers from 13 batches from the substance/substance group *Naphazoline nitrate*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Naphazoline nitrate	12I21-N05	1
Caelo	Naphazoline nitrate	18K30-B02-357305	1
Fagron	Naphazoline nitrate	21021304	1
Fagron	Naphazoline nitrate	12/21-N05	1
Fagron	Naphazoline nitrate	12J08-B40	1
Fagron	Naphazoline nitrate	140214N	1
Fagron	Naphazoline nitrate	16A14-B03-327343	1
Fagron	Naphazoline nitrate	12J08B40-294166	1
Fagron	Naphazoline nitrate	16A14-B03-322534	1
Fagron	Naphazoline nitrate	12j08-b40-303401	1
Fagron	Naphazoline nitrate	12J08-B40-294166	1
Fagron	Naphazoline nitrate	16A14-B03-333325	1
Fagron	Naphazoline nitrate	11I05-N03	1

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Naphazoline nitrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Naphazoline nitrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	13	0	111 234

The substance/substance group *Naphazoline nitrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Naphazoline nitrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sulfogaiacol hydrate	53.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Naphazoline nitrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22302	22302	0.00	72.79
24940	24940	0.00	70.25
20846	22302	5.59	69.05
21808	22302	3.53	72.21
24341	24341	0.00	79.24

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Naproxen**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22316-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Naproxen; Naproxenum

Special notes

When selecting the *Naproxen* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Naproxen	3	1	3

Second-stage model

For differentiation of the substance/substance group *Naproxen* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Naproxen*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Naproxen	15F18-B03-309492	22316	45	AR-16-FG-008486-02
Fagron	Naproxen	15F18-B03-315691	22327	45	20150703
Fagron	Naproxen	16B04-B09-326261	23105	40	20160229

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 130 spectra of 3 reference samples from the substance/substance group *Naproxen*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 559 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Naproxen*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Naproxen	17C10-B03-336472	23763	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 27 spectra from 6 *Apo-Ident* customers from 3 batches from the substance/substance group *Naproxen*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Naproxen	13E31-B40-287536	2
Fagron	Naproxen	16B04-B09-321569	24
Fagron	Naproxen	17C10-B03-336472	1

- 111 220 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Naproxen* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Naproxen* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	130	0	110 559
Type B	0	40	0	119 102
Type C	0	26	1	111 220

The substance/substance group *Naproxen* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.3846 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	96.2963 % (> 85.1852 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Naproxen* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Propranolol hydrochloride	34.71	—
Naphazoline nitrate	37.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Naproxen* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22316	22316	0.00	40.75
22327	22316	0.62	40.94
23105	22316	3.03	39.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Neomycin sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20544-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Neomycin sulfate; Neomycin sulphate; Neomycini sulfas

Special notes

When selecting the *Neomycin sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Neomycin sulfate	6	4	124

Second-stage model

For differentiation of the substance/substance group *Neomycin sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Neomycin sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Neomycin sulfate	13062923	21814	60	AR-15-FG-016581-01
Caelo	Neomycin sulfate	13062923	22276	45	20130315
Caelo	Neomycin sulfate	161650	23856	30	20160629*
Euro OTC	Neomycin sulfate	1303033-03	21771	60	AR-15-FG-016582-01
Euro OTC	Neomycin sulfate	1601046	22381	45	20160212*
Fagron	Neomycin sulfate	14C27-B05-302516	21894	60	1604527
Fagron	Neomycin sulfate	14C27-B05-302517	21961	60	20140418

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 7 reference samples from the substance/substance group *Neomycin sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 329 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 325 spectra of 7 reference samples from the substance/substance group *Neomycin sulfate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Neomycin sulfate	15237602	22389	40
Euro OTC	Neomycin sulfate	1102043-02	20758	40
Euro OTC	Neomycin sulfate	1802005	23952	40
Euro OTC	Neomycin sulfate	1903022	24642	40
Caelo	Neomycin sulfate	13062923	22276SI [†]	45
Fagron	Neomycin sulfate	14C27-B05-302516	21894SI [†]	60
Fagron	Neomycin sulfate	14C27-B05-302517	21961SI [†]	60

- 118817 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 500 spectra from 260 *Apo-Ident* customers from 131 batches from the substance/substance group *Neomycin sulfate*.
- Among them are spectra of independent samples from 124 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Neomycin sulfate	11/19-N14	1
AHD	Neomycin sulfate	14A31-B02-294698	2
AHD	Neomycin sulfate	1802005-01	2
Alliance	Neomycin sulfate	1802005-01	1
Alliance Health 13.01.204	Neomycin sulfate	1303033-01	2
Alliance Healthcare	Neomycin sulfate	1102043-03	1
apo-ident.;4,45EUR; Sanac...	Neomycin sulfate	1601046-01	1
Ashland/Sanacorp	Neomycin sulfate	1303033-02	1
aurica/phoenix	Neomycin sulfate	1102043-02	1
Caelo	Neomycin sulfate	12276405	1
Caelo	Neomycin sulfate	9105316	1
Caelo	Neomycin sulfate	10157505	5
Caelo	Neomycin sulfate	1102043-02	1
Caelo	Neomycin sulfate	24111203	1
Caelo	Neomycin sulfate	12175401	4
Caelo	Neomycin sulfate	9051402	1
Caelo	Neomycin sulfate	13062905	2
Caelo	Neomycin sulfate	563313062905	1
Caelo	Neomycin sulfate	1303033-03	2
Caelo	Neomycin sulfate	14A31-B02-294696	1
Caelo	Neomycin sulfate	13062908	1
Caelo	Neomycin sulfate	8718	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Neomycin sulfate	130303303	3
Caelo	Neomycin sulfate	1601046-01	3
Caelo	Neomycin sulfate	13062921	1
Caelo	Neomycin sulfate	16122611	2
Caelo	Neomycin sulfate	16B10-B50-328165	1
Caelo	Neomycin sulfate	161650145351	1
Caelo	Neomycin sulfate	16165008	1
Caelo	Neomycin sulfate	16165015	1
Caelo	Neomycin sulfate	1601046	1
Caelo	Neomycin sulfate	1601046-02	2
Caelo	Neomycin sulfate	18A25-B05-346135	1
Caelo	Neomycin sulfate	12276410	2
Caelo	Neomycin sulfate	13D10N05	1
Caelo	Neomycin sulfate	15298902	2
Caelo	Neomycin sulfate	18161307	2
Caelo	Neomycin sulfate	16165016	10
Caelo	Neomycin sulfate	1303033-02	1
Caelo	Neomycin sulfate	1802005-01	6
Caelo	Neomycin sulfate	180200501	1
Caelo	Neomycin sulfate	13062922	1
Caelo	Neomycin sulfate	3345	1
Caelo	Neomycin sulfate	11C21-N10	1
Caelo	Neomycin sulfate	18161305	1
Caelo	Neomycin sulfate	1502004-01	1
Caelo	Neomycin sulfate	16122612	6
Caelo	Neomycin sulfate	16165004	3
Caelo	Neomycin sulfate	16165018	6
Caelo	Neomycin sulfate	N05780	1
Caelo	Neomycin sulfate	18161303	7
Caelo	Neomycin sulfate	18018704	1
Caelo	Neomycin sulfate	15237602	6
Caelo	Neomycin sulfate	13G09-N07	1
Caelo	Neomycin sulfate	1502004-03	2
Caesar & Loretz GmbH	Neomycin sulfate	19184903	1
Caesar & Loretz GmbH, 4. . .	Neomycin sulfate	11/19-N14	1
Caesar&Loretz GmbH,18.0. . .	Neomycin sulfate	16122612	1
Caesar&loretz,AHC,05.09. . .	Neomycin sulfate	15237602	1
caesar&loretz,AHC,7.3.16	Neomycin sulfate	13062923	1
Caesar&loretz,Phoenix	Neomycin sulfate	12C13-N04	1
Caesar&Loretz/Noweda	Neomycin sulfate	15298904	1
cealo	Neomycin sulfate	1502004-03	1
Cealo/AHD	Neomycin sulfate	15J09-B04-314017	1
Eurho	Neomycin sulfate	1601046-02	1
EuRho	Neomycin sulfate	1102043-02	1
EuRho/Sanacorp	Neomycin sulfate	1102043-03	1
EuRho/Sanacorp	Neomycin sulfate	1502004-01	2
euro	Neomycin sulfate	1502004-02	2
Euro OTC	Neomycin sulfate	1502004	1
Euro OTC	Neomycin sulfate	1102043	2
Euro OTC	Neomycin sulfate	L34419	3
Euro OTC	Neomycin sulfate	1601046-01	28
Euro OTC	Neomycin sulfate	1502004-02	4
Euro OTC	Neomycin sulfate	N05780	1
Euro OTC	Neomycin sulfate	151116N	1
Euro OTC	Neomycin sulfate	1502004-03	18
Euro OTC	Neomycin sulfate	1601046-1	1
Euro OTC	Neomycin sulfate	1303033-01	10
Euro OTC	Neomycin sulfate	G73890	1
Euro OTC	Neomycin sulfate	1303033-02	14
Euro OTC	Neomycin sulfate	1303001-03	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Neomycin sulfate	160146-02	1
Euro OTC	Neomycin sulfate	1102043-02	7
Euro OTC	Neomycin sulfate	160104601	2
Euro OTC	Neomycin sulfate	16019046-01	1
Euro OTC	Neomycin sulfate	1802005-01	32
Euro OTC	Neomycin sulfate	1601045-01	1
euro//Noweda	Neomycin sulfate	1601046-02	1
Euro/Phönix	Neomycin sulfate	1502004-01	1
Euro OTC	Neomycin sulfate	1502004-01	17
Euro OTC	Neomycin sulfate	1601046-02	30
Euro OTC	Neomycin sulfate	1102043-01	3
Euro OTC	Neomycin sulfate	1102043-03	4
Fagron	Neomycin sulfate	15J09-B04	1
Fagron	Neomycin sulfate	11C21-N10	3
Fagron	Neomycin sulfate	12C13-N04	4
Fagron	Neomycin sulfate	NMZ11006K	1
Fagron	Neomycin sulfate	13D10-N05	5
Fagron	Neomycin sulfate	10121-N01	1
Fagron	Neomycin sulfate	13G09N07	2
Fagron	Neomycin sulfate	13G09-N06	1
Fagron	Neomycin sulfate	13K15-B33-288069	3
Fagron	Neomycin sulfate	13K15-B33-288073	1
Fagron	Neomycin sulfate	14A31-B02-294698	1
Fagron	Neomycin sulfate	14A31B02	2
Fagron	Neomycin sulfate	14A31-B02	2
Fagron	Neomycin sulfate	14A31-B02-302519	4
Fagron	Neomycin sulfate	14c27-B05-302516	1
Fagron	Neomycin sulfate	1502004-01	2
Fagron	Neomycin sulfate	15J27-B07	1
Fagron	Neomycin sulfate	16A20-B10-327433	2
Fagron	Neomycin sulfate	16A20-B01-327433	1
Fagron	Neomycin sulfate	100810-112-91	1
Fagron	Neomycin sulfate	18A25-B05-346136	1
Fagron	Neomycin sulfate	18G28-B05-352953	2
Fagron	Neomycin sulfate	352954	1
Fagron	Neomycin sulfate	16B10-B50-328165	7
Fagron	Neomycin sulfate	17B14-B08	1
Fagron	Neomycin sulfate	15J09-B04-314017	1
Fagron	Neomycin sulfate	14A31-B02-294696	3
Fagron	Neomycin sulfate	1502004-03	1
Fagron	Neomycin sulfate	11/19-N14	4
Fagron	Neomycin sulfate	12H23-N04	6
Fagron	Neomycin sulfate	13G09-N07	16
Fagron	Neomycin sulfate	13G09-N070129/340	1
Fagron	Neomycin sulfate	16B28-B05-352957	1
Fagron	Neomycin sulfate	18G28-B05-354472	2
Fagron	Neomycin sulfate	F08469	1
Fagron	Neomycin sulfate	13D10-N05	1
Fagron	Neomycin sulfate	F08469	1
Fagron	Neomycin sulfate	4312I-01926	1
Fagron	Neomycin sulfate	14A31-B02-296724	1
Fagron	Neomycin sulfate	15J09-B04-314015	4
Fagron	Neomycin sulfate	14A31-B02-294697	1
Fagron	Neomycin sulfate	16B10-B50	3
Fagron	Neomycin sulfate	16A20-B10-324346	1
Fagron	Neomycin sulfate	17F12-B04-340237	1
Fagron	Neomycin sulfate	15i09-B04-314015	1
Fagron	Neomycin sulfate	16A20-B10	1
Fagron	Neomycin sulfate	17B14-B08-334000	2
Fagron	Neomycin sulfate	17F12-B04	1

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Supplier	Substance	Batch	Spectra
Fagron	Neomycin sulfate	18G28-B05-352957	2
Fagron	Neomycin sulfate	12I19-N14	1
Fagron	Neomycin sulfate	14C27-B05	1
Fagron	Neomycin sulfate	15J09-B04314015	1
Fagron	Neomycin sulfate	15J09-B04-314017	4
Fagron	Neomycin sulfate	M71862	2
fargron	Neomycin sulfate	14A31-B02-294698	1
Fiebig	Neomycin sulfate	1502004-03	2
Fragon/Phoenix	Neomycin sulfate	15J09-B04_322943	1
Gehe	Neomycin sulfate	183360-0009	1
Gehe	Neomycin sulfate	194A-01926	1
GEHE	Neomycin sulfate	1502001-03	1
GEHE	Neomycin sulfate	160104602	1
GEHE	Neomycin sulfate	1802005-01	1
Gehe 23.11.18	Neomycin sulfate	1802005-01	1
Caelo	Neomycin sulfate	16122618	1
HenryLamotte	Neomycin sulfate	1502004-01	1
Jenne	Neomycin sulfate	15237602	1
Kehr	Neomycin sulfate	1601046-02	1
Fagron	Neomycin sulfate	17G05-B04	1
Land/Phönix	Neomycin sulfate	13062905	2
Noweda	Neomycin sulfate	1102043-02	1
Noweda	Neomycin sulfate	15298902	1
Pfizer USA / Phönix	Neomycin sulfate	1303033-02	1
Pfizer/Euro OCT Pharma	Neomycin sulfate	1102043-02	2
Ph/Euro	Neomycin sulfate	18020501	1
Pharmacia & Upjohn Comp...	Neomycin sulfate	16165017	1
Pharmacia & Upjohn Comp...	Neomycin sulfate	16122623	1
phnoix	Neomycin sulfate	130303301	1
Phoenix	Neomycin sulfate	1601046-02	2
phoenix 13.11.14	Neomycin sulfate	1303033-03	1
Phönix	Neomycin sulfate	13D10-N05	1
Phönix	Neomycin sulfate	1601046-02	1
Fagron	Neomycin sulfate	14A31B02294696	1
Caelo	Neomycin sulfate	16122601	2
Sanacorp	Neomycin sulfate	15298902	1
Caelo	Neomycin sulfate	5/AKD35	1
Caelo	Neomycin sulfate	5/AKD36	1
siehe WE-Prüfprotokoll	Neomycin sulfate	19/12	1
Taoasis/Phoenix	Neomycin sulfate	1502004-01	1
VDL;24.6.14; 3,55EUR	Neomycin sulfate	1303033-02	2
VDL;9.12;3,55;	Neomycin sulfate	1303033-03	1
Caelo	Neomycin sulfate	13062923	4
	Neomycin sulfate	1303033-03	1
Euro OTC	Neomycin sulfate	1303033-03	16
Fagron	Neomycin sulfate	14C27-B05-302516	2
Fagron	Neomycin sulfate	14C27-B05-302517	1
Noweda/Euro	Neomycin sulfate		1
	Neomycin sulfate	13G09-N07	1

- 110 747 spectra from 742 *Apo-Ident* customers from a total of 31 764 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Neomycin sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Neomycin sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	281	44	118 817
Type C	0	460	40	110 747

The substance/substance group *Neomycin sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	86.4615 % (> 85.5385 %)
Type C	100.0000 % (> 99.8899 %)	92.0000 % (> 91.4000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Neomycin sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium gluconate	35.46	—
Tobramycin sulfate	45.06	—
Sodium ascorbate	45.26	—
Aciclovir	52.71	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Neomycin sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21894	21894	0.00	54.21
23856	23856	0.00	54.27
21961	21771	4.82	40.82
22276	21814	2.09	40.69
22381	22381	0.00	36.00
21771	21771	0.00	39.35
21814	21814	0.00	39.90

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Neostigmine bromide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20717-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Neostigmine bromide; Neostigmini bromidum

Special notes

When selecting the *Neostigmine bromide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Neostigmine bromide	4	2	10

Second-stage model

For differentiation of the substance/substance group *Neostigmine bromide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Neostigmine bromide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Neostigmine brom...	10144105	20717	40	20100616
Caelo	Neostigmine brom...	12172304	20990	40	1403163
Caelo	Neostigmine brom...	14256802	21816	60	AR-15-FG-014460-01
Caelo	Neostigmine brom...	14256802	21816SI	60	AR-15-FG-014460-01
Caelo	Neostigmine brom...	15228101	21919	60	20151002
Caelo	Neostigmine brom...	15228101	21919SI	60	20151002

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Neostigmine bromide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 369 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Neostigmine bromide*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Neostigmine bromide	171319	23369	40
Caelo	Neostigmine bromide	17131901	23373	40
Caelo	Neostigmine bromide	171319	23369SI	40
Caelo	Neostigmine bromide	17131901	23373SI	40

- 118 982 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 23 spectra from 8 *Apo-Ident* customers from 13 batches from the substance/substance group *Neostigmine bromide*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Neostigmine bromide	12172301	1
Caelo	Neostigmine bromide	13177201	1
Caelo	Neostigmine bromide	17131901	1
Caelo	Neostigmine bromide	13177206	5
Caelo	Neostigmine bromide	13177203	2
Caelo	Neostigmine bromide	131772303A	1
Caelo	Neostigmine bromide	131772303B	1
Caelo	Neostigmine bromide	15228103	1
Gehe	Neostigmine bromide	12172301	1
Gehe	Neostigmine bromide	12172307	1
Gehe	Neostigmine bromide	13177201	1
Hetterich/Noewda	Neostigmine bromide	17131901	1
Sanacorp	Neostigmine bromide	18024902	1
Caelo	Neostigmine bromide	12172304	1
Caelo	Neostigmine bromide	15228101	1
Caelo	Neostigmine bromide	14256802	3

- 111 224 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Neostigmine bromide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Neostigmine bromide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	160	0	118 982
Type C	0	23	0	111 224

The substance/substance group *Neostigmine bromide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 73.9130 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Neostigmine bromide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ethyl hydrogen fumarate calcium	20.85	–
Griseofulvin	54.61	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Neostigmine bromide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20717	20990	2.78	64.68
20990	20990	0.00	64.25
21816	21816	0.00	56.42
21919	21816	8.80	64.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Nicotinamide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20335-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Nicotinamide; Nicotinoylamidum

Special notes

When selecting the *Nicotinamide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Nicotinamide	7	8	28

Second-stage model

For differentiation of the substance/substance group *Nicotinamide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Nicotinamide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Nicotinamide	13097506	21364	40	20130416
Caelo	Nicotinamide	163048	23038	40	20161123*
Caelo	Nicotinamide	163048	23050	40	20161123*
Euro OTC	Nicotinamide	1310025-01	21643	60	20131121
Euro OTC	Nicotinamide	1511010	22251	60	20151203*
Euro OTC	Nicotinamide	1601045	22374	60	20160210*
Euro OTC	Nicotinamide	1610019	22874	40	20161202*
Euro OTC	Nicotinamide	1906027	24799	40	20190712*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 8 reference samples from the substance/substance group *Nicotinamide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 309 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 380 spectra of 9 reference samples from the substance/substance group *Nicotinamide*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Nicotinamide	11001809	20647	40
Caelo	Nicotinamide	161136	22434	60
Caelo	Nicotinamide	173419	23785	40
Caelo	Nicotinamide	190842	24525	40
Euro OTC	Nicotinamide	1707001	23555	40
Euro OTC	Nicotinamide	1801039	23957	40
Euro OTC	Nicotinamide	1812019	24493	40
Euro OTC	Nicotinamide	2001008	25071	40
Caelo	Nicotinamide	161136	22625	40

- 118 762 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 72 spectra from 38 *Apo-Ident* customers from 31 batches from the substance/substance group *Nicotinamide*.
- Among them are spectra of independent samples from 28 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Nicotinamide	12268302	1
Caelo	Nicotinamide	13352002	1
Caelo	Nicotinamide	14246806	1
Caelo	Nicotinamide	16304803	1
Caelo	Nicotinamide	1707001-01	2
Caelo	Nicotinamide	17104108	1
Caelo	Nicotinamide	12133403	1
Caelo	Nicotinamide	13097504	1
Caelo	Nicotinamide	1511010-01	1
Caelo	Nicotinamide	1610019-01	1
DSM Nutritional Prod./ ...	Nicotinamide	1106044-01	1
Euro OTC	Nicotinamide	1108021-01	1
Euro OTC	Nicotinamide	11208021	1
Euro OTC	Nicotinamide	1610019-01	7
Euro OTC	Nicotinamide	1801039-01	5
Euro OTC	Nicotinamide	1906027-01	1
Euro OTC	Nicotinamide	1511010-01	4
Euro OTC	Nicotinamide	0P11708013	1
Euro OTC	Nicotinamide	1408019-01	2
Euro OTC	Nicotinamide	1707001-01	11
Euro OTC	Nicotinamide	1408019-19	1
Euro OTC	Nicotinamide	1503024-02	1
Euro OTC	Nicotinamide	131002501	1
Euro OTC	Nicotinamide	11401052	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Nicotinamide	1211031-02	5
Euro OTC	Nicotinamide	2610019-01	1
Euro OTC	Nicotinamide	1601045-01	4
Fagron	Nicotinamide	12J02-B03	1
Fagron	Nicotinamide	L14020084	1
Gatt-Koller	Nicotinamide	4456/10104110	1
Gatt-Koller	Nicotinamide	221406112411	1
Noweda	Nicotinamide	12133403	2
Phoenix	Nicotinamide	1211031-02	1
VDL;16.04.15;5,60EUR	Nicotinamide	1408019-01	1
Caelo	Nicotinamide	13097506	1
Euro OTC	Nicotinamide		1
Euro OTC	Nicotinamide	1310025-01	3

- 111 175 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Nicotinamide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Nicotinamide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	380	0	110 309
Type B	0	380	0	118 762
Type C	0	71	1	111 175

The substance/substance group *Nicotinamide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.4211 %)
Type C	100.0000 % (> 99.8899 %)	98.6111 % (> 94.4444 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Nicotinamide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	30.71	—
Oxytetracycline hydrochloride	57.88	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Nicotinamide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24799	24799	0.00	46.26
21364	22251	5.43	45.63
21643	22251	3.90	45.89
22251	22251	0.00	46.11
22374	22374	0.00	46.15
22874	22874	0.00	46.35
23050	23050	0.00	46.13
23038	23038	0.00	45.93

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Nicotinic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20383-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Nicotinic acid; Acidum nicotinicum

Special notes

When selecting the *Nicotinic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Nicotinic acid	3	2	3

Second-stage model

For differentiation of the substance/substance group *Nicotinic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Nicotinic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Nicotinic acid	1906026	24805	40	20190711*
Fagron	Nicotinic acid	14E01-B09-293947	21692	60	AR-15-FG-008938-01
Fagron	Nicotinic acid	16H19-B02-330121	23225	40	AR-17-FG-016013-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Nicotinic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Nicotinic acid*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Nicotinic acid	1801021	23954	40
Fagron	Nicotinic acid	18B15-B07-350570	24592	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 2 *Apo-Ident* customers from 3 batches from the substance/substance group *Nicotinic acid*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Nicotinic acid	L17120080	1
gonmisol	Nicotinic acid	17-18/NCN(P)/B/008	1
Kehr	Nicotinic acid	1801021-01	2

- 111 243 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Nicotinic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Nicotinic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	4	0	111 243

The substance/substance group *Nicotinic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Nicotinic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	56.34	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Nicotinic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21692	21692	0.00	61.36
23225	23225	0.00	59.69
24805	24805	0.00	63.77

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Non-ionic emulsifying alcohol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20467-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Non-ionic emulsifying alcohol; Alkoholes emulsificantes nonionici

Special notes

When selecting the *Non-ionic emulsifying alcohol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Non-ionic emulsifying alcohol	5	2	18

Second-stage model

For differentiation of the substance/substance group *Non-ionic emulsifying alcohol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Non-ionic emulsifying alcohol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
apomix	Non-ionic emulsi. ...	NS-8350010216	23274	40	20160718
apomix	Non-ionic emulsi. ...	NS-8350010618	24695	40	20180925
Bombastus	Non-ionic emulsi. ...	19001210	24644	40	20190221
Bombastus	Non-ionic emulsi. ...	19001210	24664	40	20190221
Caelo	Non-ionic emulsi. ...	13413001	21069	40	1405257
Caelo	Non-ionic emulsi. ...	13413001	21524	40	20140116
Caelo	Non-ionic emulsi. ...	182021	24282	40	20180725*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 7 reference samples from the substance/substance group *Non-ionic emulsifying alcohol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Non-ionic emulsifying alcohol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Non-ionic emulsifying alcohol	162231	22745	40
Caelo	Non-ionic emulsifying alcohol	171836	23576	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 52 spectra from 19 *Apo-Ident* customers from 18 batches from the substance/substance group *Non-ionic emulsifying alcohol*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Non-ionic emulsifying alcohol	3066	1
Bombastus	Non-ionic emulsifying alcohol	304997	5
Bombastus	Non-ionic emulsifying alcohol	2995568	1
Bombastus	Non-ionic emulsifying alcohol	306665	1
Bombastus	Non-ionic emulsifying alcohol	284009	2
Bombastus	Non-ionic emulsifying alcohol	278281	4
Bombastus	Non-ionic emulsifying alcohol	274059	1
Bombastus	Non-ionic emulsifying alcohol	295568	6
Bombastus	Non-ionic emulsifying alcohol	267575	2
Bombastus	Non-ionic emulsifying alcohol	306666	8
Bombastus	Non-ionic emulsifying alcohol	311625	2
Caelo	Non-ionic emulsifying alcohol	21091302	1
Caelo	Non-ionic emulsifying alcohol	14241503	1
Caelo	Non-ionic emulsifying alcohol	15287902	3
Caelo	Non-ionic emulsifying alcohol	311625	1
Caelo	Non-ionic emulsifying alcohol	12254402	1
E Plus	Non-ionic emulsifying alcohol	17043701	1
L11	Non-ionic emulsifying alcohol	17043701	1
L31	Non-ionic emulsifying alcohol	16223104	1
Bombastus	Non-ionic emulsifying alcohol	292319	8
Phönix	Non-ionic emulsifying alcohol	274059	1

- 111 195 spectra from 742 *Apo-Ident* customers from a total of 31 874 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Non-ionic emulsifying alcohol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Non-ionic emulsifying alcohol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	80	0	119 062
Type C	0	52	0	111 195

The substance/substance group *Non-ionic emulsifying alcohol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 88.4615 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Non-ionic emulsifying alcohol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Emulsifying cetostearyl alcohol (type A)	17.90	—
Cetomacrogol emulsifying wax 1000 NI	21.80	—
Magnesium stearate	36.58	—
Glycerol monostearate 60	47.26	—
Cetostearyl alcohol	47.48	—
Wool alcohols	47.80	—
Glycerol monostearate 40-55%	51.01	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Non-ionic emulsifying alcohol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21069	21069	0.00	21.80
21524	24282	4.69	25.08
23274	24282	3.09	27.74
24282	24282	0.00	28.01
24695	24282	7.83	27.99
24644	24282	7.44	27.51
24664	24282	6.76	28.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Norethisterone acetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20797-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Norethisterone acetate; Norethisteroni acetat

Special notes

When selecting the *Norethisterone acetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Norethisterone acetate	5	1	28

Second-stage model

For differentiation of the substance/substance group *Norethisterone acetate* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Norethisterone acetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Norethisterone a...	15417004	23122	40	1711489
Caelo	Norethisterone a...	182252	24395	40	20181031*
Euro OTC	Norethisterone a...	1306033-01	21627	60	1511684
Fagron	Norethisterone a...	12L14-N03	20797	40	1401558
Fagron	Norethisterone a...	17B21-B01-341608	23918	40	20170619

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Norethisterone acetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Norethisterone acetate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Norethisterone acetate	14H29-B03-325225	23171	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 36 spectra from 22 *Apo-Ident* customers from 30 batches from the substance/substance group *Norethisterone acetate*.
- Among them are spectra of independent samples from 28 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Norethisterone acetate	1306033-02	2
Bombastus	Norethisterone acetate	13J08-N04	1
Caelo	Norethisterone acetate	15417001	1
Caelo	Norethisterone acetate	16081814	1
Caelo	Norethisterone acetate	15417008	1
Caelo	Norethisterone acetate	17B21-B01-335383	1
Euro/Phönix	Norethisterone acetate	1306033-01	1
Fagron	Norethisterone acetate	22061206	1
Fagron	Norethisterone acetate	23071509	1
Fagron	Norethisterone acetate	14h29-b03-310697	1
Fagron	Norethisterone acetate	14H29-B03-302277	2
Fagron	Norethisterone acetate	14D08-B01-292738	1
Fagron	Norethisterone acetate	14d08-b01-292736	1
Fagron	Norethisterone acetate	13D19-N06	1
Fagron	Norethisterone acetate	14H29-B03-321322	1
Fagron	Norethisterone acetate	14H29-B03-325224	1
Fagron	Norethisterone acetate	18C12-B03-349111	1
Fagron	Norethisterone acetate	18C12-B03-347998	1
Fagron	Norethisterone acetate	14H29-B03-299313	1
Fagron	Norethisterone acetate	18C12-B03-354815	2
Fagron	Norethisterone acetate	18C12-B03-349157	1
Fagron	Norethisterone acetate	17B21-B01-344250	1
Fagron	Norethisterone acetate	17B21-B01-335384	1
Fagron	Norethisterone acetate	17B21-B01-341607	2
Fagron	Norethisterone acetate	13J08-N04	1
Fagron	Norethisterone acetate	17B21-B01	1
Gehe	Norethisterone acetate	15417011	1
GEHE	Norethisterone acetate	18L-14B05	1
Fagron	Norethisterone acetate	12C06-N10	2
Phönix	Norethisterone acetate	14H29-B03-315702	1
Fagron	Norethisterone acetate	17B21-B01-341608	1

- 111 211 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Norethisterone acetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Norethisterone acetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	40	0	119 102
Type C	0	35	1	111 211

The substance/substance group *Norethisterone acetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	97.2222 % (> 88.8889 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Norethisterone acetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estradiol valerate	30.86	—
Fusidic acid	35.19	—
Budesonide, micronized	36.94	105.33
Povidone iodine	39.33	—
Methylcellulose	42.14	—
Testosterone	44.39	—
⋮	⋮	⋮
Prednicarbate, micronized	>50	101.75
Triamcinolone acetonide	>50	105.01
Capsaicin	>50	118.19
Betamethasone valerate	>50	134.56
Erythromycin	>50	161.10
Dexamethasone	>50	173.15
Prednisone	>50	186.19
Prednisolone, micronized	>50	226.85

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Substanz	Distance in main model	Distance in second-stage model
Triamcinolone, micronized	>50	378.43
Heparin sodium	>50	439.49
Betamethasone, micronized	>50	457.56

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Norethisterone acetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23122	23122	0.00	34.44
24395	24395	0.00	34.79
21627	21627	0.00	34.74
23918	24395	2.08	35.24
20797	20797	0.00	34.80

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Nystatin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20116-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Nystatin; Nystatinum

Special notes

When selecting the *Nystatin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Nystatin	6	2	114

Second-stage model

For differentiation of the substance/substance group *Nystatin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Nystatin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Nystatin	AP4018717N	23985	40	20160307
Caelo	Nystatin	16272214	23711	40	20160929
Caelo	Nystatin	17025110	23984	40	20170308
Euro OTC	Nystatin	1712010-01	24103	40	1807445
Euro OTC	Nystatin	1905014	24780	40	20190709*
Fagron	Nystatin	19B28-B05-191210	24645	40	20190316

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Nystatin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 449 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Nystatin*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Nystatin	1612001-03	23727	40
Fagron	Nystatin	16L21-B01-338864	23712	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 400 spectra from 228 *Apo-Ident* customers from 116 batches from the substance/substance group *Nystatin*.
- Among them are spectra of independent samples from 114 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Nystatin	1612001-01	1
Antibiotice	Nystatin	1712010-01	2
Anzag	Nystatin	2902041-02	1
Anzag	Nystatin	1712010-01	1
ApoHo 20.6.17	Nystatin	1722	1
Bombastus	Nystatin	1212024-01	1
Caelo	Nystatin	11069706	2
Caelo	Nystatin	11069719	1
Caelo	Nystatin	11069730	1
Caelo	Nystatin	12017009	1
Caelo	Nystatin	C129330	1
Caelo	Nystatin	3101201	1
Caelo	Nystatin	13101202	1
Caelo	Nystatin	13101201	1
Caelo	Nystatin	11069704	1
Caelo	Nystatin	12017011	2
Caelo	Nystatin	12158006	7
Caelo	Nystatin	12017010	1
Caelo	Nystatin	12158004	3
Caelo	Nystatin	12017015	2
Caelo	Nystatin	12158019	3
Caelo	Nystatin	12158005	1
Caelo	Nystatin	6082013B	1
Caelo	Nystatin	12158009	1
Caelo	Nystatin	2091304	1
Caelo	Nystatin	13173401	8
Caelo	Nystatin	12138021	2
Caelo	Nystatin	13173408	1
Caelo	Nystatin	14363514	1
Caelo	Nystatin	15335310	1
Caelo	Nystatin	18072114	8
Caelo	Nystatin	18072112	3
Caelo	Nystatin	18072123	8
Caelo	Nystatin	18072120	4
Caelo	Nystatin	18072121	3
Caelo	Nystatin	18072118	1

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Supplier	Substance	Batch	Spectra
Caelo	Nystatin	18072126	1
Caelo	Nystatin	19028808	4
Caelo	Nystatin	19028806	1
Caelo	Nystatin	11069731	1
Caelo	Nystatin	18072128	2
Caelo	Nystatin	12017004	4
Caelo	Nystatin	12158004	1
Caelo	Nystatin	18072108	4
Caelo	Nystatin	12017003	1
Caelo	Nystatin	12158010	4
Caelo	Nystatin	12158020	1
Caelo	Nystatin	1(18072128)	1
Caelo	Nystatin	1712010-01	6
Caelo	Nystatin	19028809	3
Caelo	Nystatin	81072113	1
Caelo	Nystatin	3338	1
Caelo	Nystatin	18072124	7
Caelo	Nystatin	19028803	1
Caelo	Nystatin	1612001-03	1
Caelo	Nystatin	12158022	1
Caelo	Nystatin	18072129	2
Caelo	Nystatin	18072105	3
Caelo	Nystatin	1107046-01	1
Caelo	Nystatin	11069716	1
Caelo	Nystatin	12158008	3
Caelo	Nystatin	18072014	1
Caelo	Nystatin	19028801	6
Caelo	Nystatin	18072109	7
Caelo	Nystatin	18072113	11
Caelo	Nystatin	121580921	1
Caesar & Loretz GmbH	Nystatin	18072113	3
Caesar & Loretz GmbH	Nystatin	19028801	3
Caesar & Loretz GmbH / ...	Nystatin	18072124	1
Caesar & Loretz GmbH/An...	Nystatin	19028809	1
Caesar & Loretz GmbH/Ge...	Nystatin	19028808	1
Caesar&Lorenz / Gehe	Nystatin	19028810	1
Caesar&lorenz,AHC	Nystatin	14196509	2
Caesar&lorenz,Anzag	Nystatin	12158008	3
Caesar&lorenz,Phoenix	Nystatin	1111057-01	3
Caesar&lorenz,Phoenix	Nystatin	1218008	1
Caesar&lorenz,Phoenix	Nystatin	13173401	4
Caesar&lorenz,Phoenix	Nystatin	13173408	1
Caesar&lorenz,Phoenix	Nystatin	14363512	1
Canea Pharma GmbH	Nystatin	18072121	1
Cealo/Alliance Healthcare	Nystatin	18072118	1
DSM Căiua S.p.A	Nystatin	1207009-01	1
EuRho	Nystatin	1107046-01	1
EuRho	Nystatin	1207009-01	1
EuRho/Anzag	Nystatin	1107036-01	1
EuRho/Phoenix	Nystatin	1712010-01	2
Euro OTC	Nystatin	1612001-03	4
Euro OTC	Nystatin	16120001-02	1
Euro OTC	Nystatin	19500711	1
Euro OTC	Nystatin	4014991	1
Euro OTC	Nystatin	1111057-01	4
Euro OTC	Nystatin	1207009-01	7
Euro OTC	Nystatin	127009-02	1
Euro OTC	Nystatin	161200103	2
Euro OTC	Nystatin	1307053-01	5
Euro OTC	Nystatin	1207009-02	2

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Supplier	Substance	Batch	Spectra
Euro OTC	Nystatin	1212024-02	13
Euro OTC	Nystatin	C129854	1
Euro OTC	Nystatin	1511020-01	1
Euro OTC	Nystatin	1307053-02	2
Euro OTC	Nystatin	1511020-02	1
Euro OTC	Nystatin	1712010-02	17
Euro OTC	Nystatin	1107046-01	2
Euro OTC	Nystatin	130705301	1
Euro OTC	Nystatin	1107036-01	4
Euro OTC	Nystatin	1905014-01	12
Euro OTC	Nystatin	1712010	1
Euro OTC	Nystatin	702270	1
Euro OTC	Nystatin	C129531	2
EUro/AHD	Nystatin	1307053-01	1
Euro/Gehe	Nystatin	1905014-01	1
Euro OTC	Nystatin	1212024-01	14
Euro OTC	Nystatin	4019851	2
Euro OTC	Nystatin	2811032-01	1
Euro OTC	Nystatin	190501401	1
Euro OTC	Nystatin	121024-01	1
Europharm/Otto	Nystatin	1107046-01	1
Fagron	Nystatin	20121202	1
Fagron	Nystatin	4014376	1
Fagron	Nystatin	19B28-B05-191208	1
Fagron	Nystatin	12C29-N09	1
Fagron	Nystatin	11K11-No4	1
Fagron	Nystatin	11C21-N10	1
Fagron	Nystatin	17J25-B01-348043	1
Fagron	Nystatin	18072112	1
Fagron	Nystatin	12G04-N12	1
Fagron	Nystatin	13C11-N08	1
Gatt-Koller	Nystatin	1900206	2
Gehe	Nystatin	1207009-01	1
Gehe	Nystatin	1111057-01	1
Gehe	Nystatin	1107036-01	1
Gehe	Nystatin	12158008	1
Gehe	Nystatin	1307053-02	1
Gehe	Nystatin	1712010-02	1
Gehe	Nystatin	1712010-01	1
Gehe	Nystatin	1905014-01	1
Euro OTC	Nystatin	171201001	1
Euro OTC	Nystatin	171201002	4
Kehr	Nystatin	1612001-02	1
Kehr	Nystatin	18072123	1
L12	Nystatin	1712010-01	1
Nachprüfung	Nystatin	1118E-01941	1
Nachprüfung	Nystatin	123456	1
Noweda	Nystatin	1207009-01	1
Noweda	Nystatin	19028801	1
Euro OTC	Nystatin	C129440	1
Phoenix	Nystatin	1712010-01	1
Phoenix	Nystatin	1712010-02	1
Phoenix	Nystatin	3361	1
Phoenix	Nystatin	3410	1
Phoenix	Nystatin	1905014-01	1
Caelo	Nystatin	19026806	1
Phönix	Nystatin	12017005	2
Phönix	Nystatin	1212024-01	1
Phönix	Nystatin	1212024-02	1
Phönix	Nystatin	12158010	1

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Supplier	Substance	Batch	Spectra
Phönix	Nystatin	18072109	1
Phönix	Nystatin	1905014-01	1
Caelo	Nystatin	19028813	1
Phönix/Euro	Nystatin	1111057-01	1
Sanacorp	Nystatin	1107046-01	1
Sanacorp	Nystatin	1212024-02	1
Caelo	Nystatin	12158021	2
Euro OTC	Nystatin	1712010-01	45
Euro OTC	Nystatin	1905014	1

- 110847 spectra from 742 *Apo-Ident* customers from a total of 31 777 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Nystatin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Nystatin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	341	59	110 847

The substance/substance group *Nystatin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	85.2500 % (> 84.5000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Nystatin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bacitracin	19.47	—
Escin, water-soluble	26.12	—
Colistin sulfate	33.78	—
Amphotericin B	40.83	—
Citrulline	41.44	—
Calcium citrate tetrahydrate	43.33	—
alpha-tocopheryl acetate dry concentrate	44.24	—
Thiamine chloride hydrochloride	44.82	—
Glycyrrhizic acid	46.86	—
Polymyxin B sulfate	47.68	—
Cyanocobalamin	48.22	—
Menthol	50.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Nystatin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23711	24103	4.91	19.89
23984	24103	5.38	20.42
23985	24103	8.96	20.85
24103	24103	0.00	19.59
24780	24780	0.00	19.47
24645	24103	5.11	20.60

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Octenidine dihydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20759-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Octenidine dihydrochloride; Octenidini dihydrochloridum

Special notes

When selecting the *Octenidine dihydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Octenidine dihydrochloride	8	2	109

Second-stage model

For differentiation of the substance/substance group *Octenidine dihydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Octenidine dihydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Octenidine dihyd...	12115202	20759	40	20120511
Caelo	Octenidine dihyd...	13071407	20988	40	1407345
Caelo	Octenidine dihyd...	13166806	21331	40	20130718
Caelo	Octenidine dihyd...	15275502	21888	60	20150910
Caelo	Octenidine dihyd...	15356601	21947	60	1604116
Caelo	Octenidine dihyd...	15356601	21947SI	60	1604116
Caelo	Octenidine dihyd...	170423	23307	40	20170214*
Caelo	Octenidine dihyd...	170423	23307SI	40	20170214*
Caelo	Octenidine dihyd...	163355	23309	40	20170403*
Caelo	Octenidine dihyd...	18223413	24597	40	20181005
Caelo	Octenidine dihyd...	18223413	24597SI	40	20181005

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 11 reference samples from the substance/substance group *Octenidine dihydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 189 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 240 spectra of 5 reference samples from the substance/substance group *Octenidine dihydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Octenidine dihydrochloride	160330	22485	60
Caelo	Octenidine dihydrochloride	180174	24023	40
Caelo	Octenidine dihydrochloride	15275502	21888SI [†]	60
Caelo	Octenidine dihydrochloride	163355	23309SI [†]	40
Caelo	Octenidine dihydrochloride	180174	24023SI	40

- 118 902 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 734 spectra from 301 *Apo-Ident* customers from 112 batches from the substance/substance group *Octenidine dihydrochloride*.
- Among them are spectra of independent samples from 109 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Octenidine dihydrochloride	18A12-B03-346964	1
AHD	Octenidine dihydrochloride	18197504	1
Alliance Healthcare	Octenidine dihydrochloride	18223403	3
Alliance Healthcare	Octenidine dihydrochloride	18223415	1
Anzag	Octenidine dihydrochloride	17042602	1
Euro OTC	Octenidine dihydrochloride	18223413	4
Apomix/Noweda	Octenidine dihydrochloride	13166813	1
Audor Pharma	Octenidine dihydrochloride	17042304	1
Bombastus	Octenidine dihydrochloride	18017402	1
Caelo	Octenidine dihydrochloride	17042305	5
Caelo	Octenidine dihydrochloride	15006207	5
Caelo	Octenidine dihydrochloride	15275504	1
Caelo	Octenidine dihydrochloride	15356603	3
Caelo	Octenidine dihydrochloride	8724	1
Caelo	Octenidine dihydrochloride	15356703	9
Caelo	Octenidine dihydrochloride	16032803	7
Caelo	Octenidine dihydrochloride	152755020	1
Caelo	Octenidine dihydrochloride	16033002	2
Caelo	Octenidine dihydrochloride	16032909	7
Caelo	Octenidine dihydrochloride	16277802	8
Caelo	Octenidine dihydrochloride	16325406	6

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Octenidine dihydrochloride	6325305	1
Caelo	Octenidine dihydrochloride	16325305	10
Caelo	Octenidine dihydrochloride	17042602	7
Caelo	Octenidine dihydrochloride	17042903	18
Caelo	Octenidine dihydrochloride	17042303	4
Caelo	Octenidine dihydrochloride	16335510	7
Caelo	Octenidine dihydrochloride	172118501	1
Caelo	Octenidine dihydrochloride	17218503	10
Caelo	Octenidine dihydrochloride	17042501	1
Caelo	Octenidine dihydrochloride	172185035514	1
Caelo	Octenidine dihydrochloride	17218504	1
Caelo	Octenidine dihydrochloride	16335506	1
Caelo	Octenidine dihydrochloride	17218051	1
Caelo	Octenidine dihydrochloride	11071925	1
Caelo	Octenidine dihydrochloride	18017402	48
Caelo	Octenidine dihydrochloride	13061801	1
Caelo	Octenidine dihydrochloride	300718A	1
Caelo	Octenidine dihydrochloride	17218907	1
Caelo	Octenidine dihydrochloride	18197502	13
Caelo	Octenidine dihydrochloride	18223403	34
Caelo	Octenidine dihydrochloride	18223418	1
Caelo	Octenidine dihydrochloride	18223415	12
Caelo	Octenidine dihydrochloride	18223424	13
Caelo	Octenidine dihydrochloride	18223423	14
Caelo	Octenidine dihydrochloride	18233427	1
Caelo	Octenidine dihydrochloride	16335508	5
Caelo	Octenidine dihydrochloride	1711160HC/16335509	1
Caelo	Octenidine dihydrochloride	17218508	22
Caelo	Octenidine dihydrochloride	18223426	4
Caelo	Octenidine dihydrochloride	16335509	10
Caelo	Octenidine dihydrochloride	1728506	1
Caelo	Octenidine dihydrochloride	18197504	7
Caelo	Octenidine dihydrochloride	18223404	13
Caelo	Octenidine dihydrochloride	18223427	5
Caelo	Octenidine dihydrochloride	2(18223413)	1
Caelo	Octenidine dihydrochloride	16032901	2
Caelo	Octenidine dihydrochloride	13166808	2
Caelo	Octenidine dihydrochloride	13166810	1
Caelo	Octenidine dihydrochloride	16325410	2
Caelo	Octenidine dihydrochloride	18223407	6
Caelo	Octenidine dihydrochloride	3277	1
Caelo	Octenidine dihydrochloride	3329	1
Caelo	Octenidine dihydrochloride	16033001	2
Caelo	Octenidine dihydrochloride	17042302	7
Caelo	Octenidine dihydrochloride	18223409	22
Caelo	Octenidine dihydrochloride	18223416	12
Caelo	Octenidine dihydrochloride	16335507	7
Caelo	Octenidine dihydrochloride	1515E-03732	1
Caelo	Octenidine dihydrochloride	816M-03732	1
Caelo	Octenidine dihydrochloride	18223411	12
Caelo	Octenidine dihydrochloride	15006202	3
Caelo	Octenidine dihydrochloride	16032903	2
Caelo	Octenidine dihydrochloride	17218501	29
Caelo	Octenidine dihydrochloride	16325408	2
Caelo	Octenidine dihydrochloride	17218506	21
Caelo	Octenidine dihydrochloride	18223414	2
Caelo	Octenidine dihydrochloride	17042304	12
Caelo	Octenidine dihydrochloride	16335502	3
Caelo	Octenidine dihydrochloride	16335504	15
Caelo	Octenidine dihydrochloride	17218507	8

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Supplier	Substance	Batch	Spectra
Caelo	Octenidine dihydrochloride	17218509	23
Caelo	Octenidine dihydrochloride	18197501	31
Caelo	Octenidine dihydrochloride	15275503	3
Caelo	Octenidine dihydrochloride	18223419	4
Caelo	Octenidine dihydrochloride	20000606002	1
Caelo	Octenidine dihydrochloride	16032910	5
Caelo	Octenidine dihydrochloride	16325304	10
Caelo	Octenidine dihydrochloride	16325202	1
Caelo	Octenidine dihydrochloride	17042701	1
Caelo	Octenidine dihydrochloride	181975025789	1
Caelo	Octenidine dihydrochloride	13166801	1
Caelo	Octenidine dihydrochloride	15006203	1
Caelo	Octenidine dihydrochloride	16302910	1
Caelo	Octenidine dihydrochloride	190118-03	1
Caelo	Octenidine dihydrochloride	18223428	1
Caelo	Octenidine dihydrochloride	16335505	4
Caesar & Lorenz GmbH	Octenidine dihydrochloride	17218503	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	15006210	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	17218509	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	181975002	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223411	3
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223413	2
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223420	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223403	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223423	1
Caesar & Loretz GmbH	Octenidine dihydrochloride	18223428	1
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	16325305	1
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18223403	2
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18223415	2
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18223428	1
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18233415	1
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18223416	1
Caesar & Loretz GmbH / ...	Octenidine dihydrochloride	18223426	1
Caesar & Loretz GmbH / G	Octenidine dihydrochloride	18223404	1
Caesar & Loretz GmbH/Fi...	Octenidine dihydrochloride	18223423	1
Caesar&Lorenz / Gehe	Octenidine dihydrochloride	18223419	1
Caesar&Loretz GmbH	Octenidine dihydrochloride	16335504	1
Caesar&Loretz GmbH, 14...	Octenidine dihydrochloride	17042302	1
Cealo	Octenidine dihydrochloride	17218507	1
Cealo/Sanacorp	Octenidine dihydrochloride	15006207	1
Cealo/Sanacorp	Octenidine dihydrochloride	16325305	1
Ceasar & Loretz GmbH / ...	Octenidine dihydrochloride	16335509	1
Celo	Octenidine dihydrochloride	16277802	1
EuRho/Sanacorp	Octenidine dihydrochloride	16335508	1
Euro OTC	Octenidine dihydrochloride	17218501	1
Euro OTC	Octenidine dihydrochloride	18197502	2
Euro OTC	Octenidine dihydrochloride	16032803	1
Euro OTC	Octenidine dihydrochloride	18223404	1
Fagron	Octenidine dihydrochloride	16335507	1
Fagron	Octenidine dihydrochloride	18223403	1
Fagron	Octenidine dihydrochloride	15356601	1
Fagron	Octenidine dihydrochloride	15356703	1
Fagron	Octenidine dihydrochloride	187223403	1
Fagron	Octenidine dihydrochloride	16277802	1
Fagron	Octenidine dihydrochloride	16335510	1
Fiebig	Octenidine dihydrochloride	18017402	1
Fresenius	Octenidine dihydrochloride	60715101	1
Gehe	Octenidine dihydrochloride	17042903	1
Gehe	Octenidine dihydrochloride	17218501	1
Gehe	Octenidine dihydrochloride	172218508	1

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Supplier	Substance	Batch	Spectra
Gehe	Octenidine dihydrochloride	17218508	1
Gehe	Octenidine dihydrochloride	18017402	2
Gehe	Octenidine dihydrochloride	18223401	1
Gehe	Octenidine dihydrochloride	18223403	1
Gehe	Octenidine dihydrochloride	18223424	1
GEHE	Octenidine dihydrochloride	16325304	1
GEHE	Octenidine dihydrochloride	16325305	1
GEHE	Octenidine dihydrochloride	17218509	1
Gehe 21-01-2019	Octenidine dihydrochloride	18223403	1
Bombastus	Octenidine dihydrochloride	17218506	1
Hepart	Octenidine dihydrochloride	17218508	1
Jenne	Octenidine dihydrochloride	17218507	1
Jenne	Octenidine dihydrochloride	18197502	2
JENNE	Octenidine dihydrochloride	17218508	1
Kehr	Octenidine dihydrochloride	17218508	1
Krieger	Octenidine dihydrochloride	3132	1
Löwen City-Apotheke Bar...	Octenidine dihydrochloride	2042015	1
Noweda	Octenidine dihydrochloride	16335507	1
Caelo	Octenidine dihydrochloride	16032902	4
Pheonix	Octenidine dihydrochloride	17218509	1
Phoenix	Octenidine dihydrochloride	3033	1
Phoenix	Octenidine dihydrochloride	3040	1
Phoenix	Octenidine dihydrochloride	3107	1
Phoenix	Octenidine dihydrochloride	3113	1
Phoenix	Octenidine dihydrochloride	17218506	1
Phoenix	Octenidine dihydrochloride	3221	1
Phoenix	Octenidine dihydrochloride	18223415	2
Phoenix	Octenidine dihydrochloride	3419	1
Phoenix	Octenidine dihydrochloride	3423	1
Phönix	Octenidine dihydrochloride	3155	1
Phönix	Octenidine dihydrochloride	17218506	1
Sanacorp	Octenidine dihydrochloride	16335504	1
Caelo	Octenidine dihydrochloride	18223413	27
Caelo	Octenidine dihydrochloride	15275502	7
Caelo	Octenidine dihydrochloride	15356601	6

- 110 513 spectra from 742 *Apo-Ident* customers from a total of 31 781 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Octenidine dihydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Octenidine dihydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	500	0	110 189
Type B	0	240	0	118 902
Type C	0	712	22	110 513

The substance/substance group *Octenidine dihydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	97.0027 % (> 96.5940 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Octenidine dihydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estriol	82.46	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Octenidine dihydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21888	21947	2.24	83.19
21947	21947	0.00	85.15
24597	23309	12.60	85.80
20759	20988	3.67	85.03
20988	20988	0.00	82.46
21331	21947	9.05	88.76
23309	23309	0.00	85.21
23307	23307	0.00	91.12

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ofloxacin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21047-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ofloxacin; Ofloxacinum

Special notes

When selecting the *Ofloxacin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ofloxacin	4	1	4

Second-stage model

For differentiation of the substance/substance group *Ofloxacin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ofloxacin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Ofloxacin	13A17-N01	21047	40	1403155
Fagron	Ofloxacin	13A17-N01	21052	40	20130123
Fagron	Ofloxacin	13A17-N01	21811	60	20130123
Fagron	Ofloxacin	15H19-B01-312926	21918	60	20151006
Fagron	Ofloxacin	15H19-B01-325226	23090	40	1707611
Fagron	Ofloxacin	18J30-B01-360431	24598	40	20190419

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Ofloxacin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 409 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 310 spectra of 7 reference samples from the substance/substance group *Ofloxacin*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Ofloxacin	15H19-B01-337265	23753	40
Fagron	Ofloxacin	13A17-N01	21811SI [†]	60
Fagron	Ofloxacin	15H19-B01-312926	21918SI [†]	60
Fagron	Ofloxacin	15H19-B01-325226	23090SI [†]	30
Fagron	Ofloxacin	15H19-B01-337265	23753SI	40
Fagron	Ofloxacin	15H19-B01-337265	23754	40
Fagron	Ofloxacin	15H19-B01-337265	23754SI	40

- 118 832 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 5 *Apo-Ident* customers from 5 batches from the substance/substance group *Ofloxacin*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Ofloxacin	15H19-B01	1
Fagron	Ofloxacin	15H1-OF-M20150401B	1
Fagron	Ofloxacin	15H19-B01-314470	1
Fagron	Ofloxacin	15H19-B01-343412	1
Fagron	Ofloxacin	13A17-N01	2

- 111 241 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ofloxacin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ofloxacin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	304	6	118 832
Type C	0	6	0	111 241

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

The substance/substance group *Ofloxacin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	98.0645 % (> 97.0968 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ofloxacin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pilocarpine hydrochloride	56.26	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ofloxacin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21047	21047	0.00	61.90
21052	21047	1.31	62.04
21811	23090	9.22	58.72
21918	23090	7.51	57.37
23090	23090	0.00	61.80
24598	21047	6.92	60.86

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Omeprazole**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21098-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Omeprazole; Omeprazolum

Special notes

When selecting the *Omeprazole* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Omeprazole	3	2	24

Second-stage model

For differentiation of the substance/substance group *Omeprazole* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Omeprazole*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Omeprazole	15K12-B02-314608	22740	40	20151124
Fagron	Omeprazole	15K12-B02-314608	22890	40	20151124
Fagron	Omeprazole	19F14-B01-362735	24768	40	1910227
Inresa	Omeprazole	OPFP14017	21787	60	1507407
Inresa	Omeprazole	OPFP14017	21796	60	20140228
Inresa	Omeprazole	OPFP14017	22284	60	20140528
Inresa	Omeprazole	OPFP14017	23273	40	20150428

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Omeprazole*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 349 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Omeprazole*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Omeprazole	16I20-B03-328940	23272	40
Fagron	Omeprazole	18K01-B03-358185	24583	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 83 spectra from 37 *Apo-Ident* customers from 29 batches from the substance/substance group *Omeprazole*.
- Among them are spectra of independent samples from 24 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Omeprazole	16I20-B03-328940	3
Fagron	Omeprazole	18E22B03353496	1
Caelo	Omeprazole	18K01-B03-358185	1
Caelo	Omeprazole	16I20-B03-329040	1
Caelo	Omeprazole	15K12B02314608	1
Caelo	Omeprazole	18E22-B03-353496	1
Caelo	Omeprazole	17H15-B03-340200	1
Caelo	Omeprazole	17H15-B03	1
Caelo	Omeprazole	17K28-B07-348698	6
Fagron	Omeprazole	15K12-B02	2
Fagron	Omeprazole	15k12-B02	1
Fagron	Omeprazole	15K12-B02-525174	2
Fagron	Omeprazole	OPFP16030	1
Fagron	Omeprazole	16I20-B03-328940	1
Fagron	Omeprazole	17H15-B03-340200	1
Fagron	Omeprazole	17h15b0334821	1
Fagron	Omeprazole	17H15-B03	1
Fagron	Omeprazole	17h15-b03-342821	1
Fagron	Omeprazole	17B28-B02	1
Fagron	Omeprazole	18K01-B03-358185	6
Fagron	Omeprazole	19F14-B01-363425	2
Fagron	Omeprazole	17B28-B02-525511	1
Fagron	Omeprazole	17B28-B02-525557	1
Fagron	Omeprazole	OPFP19002	1
Fagron	Omeprazole	15B26-B40-305669	2
Fagron	Omeprazole	16/20-B03-328940	3
Fagron	Omeprazole	17H15-B03-342821	9
Fagron	Omeprazole	17K28-B07-348698	7
Fagron	Omeprazole	18E22-B03-353496	5
Fagron	Omeprazole	16B16-B01-52535	1
Noweda	Omeprazole	15K15-B02-314608	1
Noweda	Omeprazole	17H15-B03-342821	3
Phoenix	Omeprazole	18E22-B03-353496	4
Phönix	Omeprazole	17K28-B07-348698	2
Sanacorp	Omeprazole	17H15-B03-342821	1
Fagron	Omeprazole	19F14-B01-362735	2
Fagron	Omeprazole	15K12-B02-314608	3
Fagron	Omeprazole		1

- 111 164 spectra from 742 *Apo-Ident* customers from a total of 31 862 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Omeprazole* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Omeprazole* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	80	0	119 062
Type C	0	83	0	111 164

The substance/substance group *Omeprazole* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 92.7711 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Omeprazole* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cyproterone acetate	28.86	—
Naphazoline hydrochloride	30.30	—
Diltiazem hydrochloride	39.07	—
Diphenhydramine hydrochloride	42.19	—
Glycine	44.36	—
Griseofulvin	45.72	—
Benzylamine hydrochloride	49.71	—
Cocaine hydrochloride	56.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Omeprazole* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24768	24768	0.00	50.60
21787	21787	0.00	45.10
21796	21787	3.78	45.07
22284	21787	1.76	43.83
22740	21787	3.93	43.59
22890	21787	3.73	46.69
23273	21787	4.13	45.46

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ornithine aspartate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20842-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ornithine aspartate; Ornithinum asparticum

Special notes

When selecting the *Ornithine aspartate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ornithine aspartate	7	3	0

Second-stage model

For differentiation of the substance/substance group *Ornithine aspartate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ornithine aspartate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Ornithine aspart...	L1304034-01	20842	40	1402571
Euro OTC	Ornithine aspart...	1312030-01	21710	60	1506280
Euro OTC	Ornithine aspart...	1611018	22924	40	20161213*
Euro OTC	Ornithine aspart...	1611018-01	23198	40	20161213
Fagron	Ornithine aspart...	14A20-B07-296093	21694	45	1506279
Fagron	Ornithine aspart...	14I24-B04-307758	22599	40	20141110
Fagron	Ornithine aspart...	14I24-B04-307758	22600	40	20141110
Fagron	Ornithine aspart...	17I21-B05-342561	23864	40	1804455

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 345 spectra of 8 reference samples from the substance/substance group *Ornithine aspartate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 344 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Ornithine aspartate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Ornithine aspartate	1711015	23899	40
Euro OTC	Ornithine aspartate	1805026	24125	40
Euro OTC	Ornithine aspartate	1907037	24859	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Ornithine aspartate*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ornithine aspartate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ornithine aspartate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	345	0	110 344
Type B	0	120	0	119 022
Type C	0	0	0	111 247

The substance/substance group *Ornithine aspartate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2609 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ornithine aspartate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Captopril	48.84	—
Choline hydrogen tartrate	57.23	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ornithine aspartate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22599	21694	3.15	72.17
22924	22924	0.00	71.29
21694	21694	0.00	75.66
21710	21710	0.00	63.80
23198	21694	7.28	72.40
23864	23864	0.00	62.78
22600	21710	2.79	64.44
20842	20842	0.00	56.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ornithine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20389-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ornithine hydrochloride; Ornithinum hydrochloricum

Special notes

When selecting the *Ornithine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ornithine hydrochloride	4	5	6

Second-stage model

For differentiation of the substance/substance group *Ornithine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ornithine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Ornithine hydroc...	1307028-01	21622	120	20130813
Euro OTC	Ornithine hydroc...	1605011	22573	40	20160601*
Euro OTC	Ornithine hydroc...	2001004	25084	40	20200123*
Fagron	Ornithine hydroc...	13A03-N05	20967	40	1403094

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 4 reference samples from the substance/substance group *Ornithine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Ornithine hydrochloride*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Ornithine hydrochloride	1612009	22923	40
Euro OTC	Ornithine hydrochloride	1612009-01	23009	40
Euro OTC	Ornithine hydrochloride	1704006	23159	40
Euro OTC	Ornithine hydrochloride	1803018	24085	40
Euro OTC	Ornithine hydrochloride	1906015	24810	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 7 spectra from 3 *Apo-Ident* customers from 7 batches from the substance/substance group *Ornithine hydrochloride*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Ornithine hydrochloride	315E-03475	1
Euro OTC	Ornithine hydrochloride	1704006-01	1
Euro OTC	Ornithine hydrochloride	4712A-03475	1
Euro OTC	Ornithine hydrochloride	1014I-03475	1
Euro OTC	Ornithine hydrochloride	516Q-03475	1
Fagron	Ornithine hydrochloride	15A13-B03	1
Fagron	Ornithine hydrochloride	13A03-N05	1

- 111 240 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ornithine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ornithine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	200	0	118 942
Type C	0	7	0	111 240

The substance/substance group *Ornithine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ornithine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	49.40	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ornithine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22573	22573	0.00	81.50
20967	20967	0.00	79.80
21622	22573	1.54	81.44
25084	25084	0.00	79.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Oxalic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20458-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Oxalic acid; Acidum oxalicum cryst.

Special notes

When selecting the *Oxalic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Oxalic acid	5	1	23

Second-stage model

For differentiation of the substance/substance group *Oxalic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oxalic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Oxalic acid	13353901	21042	40	20131029
Caelo	Oxalic acid	12212410	21066	40	1403223
Caelo	Oxalic acid	13353918	21774	60	20131029
Caelo	Oxalic acid	171140	23287	40	20170426*
Caelo	Oxalic acid	171140	23688	40	20170426*
Caelo	Oxalic acid	18202403	24428	40	1905160

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Oxalic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 60 spectra of 1 reference samples from the substance/substance group *Oxalic acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Oxalic acid	13353905	21453	60

- 119 082 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 27 spectra from 22 *Apo-Ident* customers from 25 batches from the substance/substance group *Oxalic acid*.
- Among them are spectra of independent samples from 23 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Oxalic acid	12212407	1
Caelo	Oxalic acid	12212406	1
Caelo	Oxalic acid	13353907	2
Caelo	Oxalic acid	13353910	1
Caelo	Oxalic acid	10383104	1
Caelo	Oxalic acid	13195414	1
Caelo	Oxalic acid	11111703	1
Caelo	Oxalic acid	17114003	1
Caelo	Oxalic acid	16050205	1
Caelo	Oxalic acid	7111808	1
Caelo	Oxalic acid	Retest17111401	1
Caelo	Oxalic acid	17344503	1
Caelo	Oxalic acid	12147010	1
Caelo	Oxalic acid	4812U-01039	1
Caelo	Oxalic acid	914E-01039	1
Caelo	Oxalic acid	12212411	1
Caelo	Oxalic acid	13353905	2
Caelo	Oxalic acid	13353915	1
Caelo	Oxalic acid	16297401	1
Caelo	Oxalic acid	14334703	1
Caelo	Oxalic acid	13195413	1
Caesar&Loretz GmbH/ All...	Oxalic acid	13353920	1
sanacorp	Oxalic acid	11098213	1
Caelo	Oxalic acid	13353901	1
Nachprüfung	Oxalic acid		1

- 111 220 spectra from 742 *Apo-Ident* customers from a total of 31 867 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Oxalic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oxalic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	253	7	110 429
Type B	0	60	0	119 082
Type C	0	17	10	111 220

The substance/substance group *Oxalic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	97.3077 % (> 96.1538 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 90.0000 %)
Type C	100.0000 % (> 99.8899 %)	62.9630 % (> 51.8519 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Oxalic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	46.50	—
Bismuth gallath, basic	51.00	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oxalic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21042	21066	4.37	51.57
21066	21066	0.00	55.70
21774	21066	4.44	52.12
23287	23287	0.00	54.55
23688	23688	0.00	55.82
24428	24428	0.00	44.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Oxetacaine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 23686-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Oxetacaine; Oxetacainum

Special notes

When selecting the *Oxetacaine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Oxetacaine	3	1	4

Second-stage model

For differentiation of the substance/substance group *Oxetacaine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oxetacaine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Oxetacaine	AP010-160120	24104	40	1809415
Caelo	Oxetacaine	172498	23686	40	20170925*
Caelo	Oxetacaine	191134	24757	40	20190523*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Oxetacaine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 50 spectra of 1 reference samples from the substance/substance group *Oxetacaine*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Oxetacaine	17249805	23916	50

- 119 092 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 6 spectra from 6 *Apo-Ident* customers from 4 batches from the substance/substance group *Oxetacaine*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Oxetacaine	17249810	3
Caelo	Oxetacaine	19113402	1
Kehr	Oxetacaine	17249805	1
Caelo	Oxetacaine	19113401	1

- 111 241 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Oxetacaine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oxetacaine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	50	0	119 092
Type C	0	5	1	111 241

The substance/substance group *Oxetacaine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 88.0000 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Oxetacaine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Atropine sulfate	39.05	—
Sildenafil citrate	50.60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oxetacaine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24757	24757	0.00	42.54
23686	23686	0.00	42.56
24104	24104	0.00	42.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Oxybuprocaine hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20958-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Oxybuprocaine hydrochloride; Oxybuprocaini hydrochloridum

Special notes

When selecting the *Oxybuprocaine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Oxybuprocaine hydrochloride	5	1	9

Second-stage model

For differentiation of the substance/substance group *Oxybuprocaine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oxybuprocaine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Oxybuprocaine hy...	13D16-N12	20958	40	1402060
Fagron	Oxybuprocaine hy...	13J24-B07-295015	21799	60	AR-15-FG-014812-02
Fagron	Oxybuprocaine hy...	15A26-B07-306787	21922	60	20150203
Fagron	Oxybuprocaine hy...	17G21-B03-338576	23745	40	20170823
Fagron	Oxybuprocaine hy...	16L05-B06-334330	23752	40	20170113

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Oxybuprocaine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 5 reference samples from the substance/substance group *Oxybuprocaine hydrochloride*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Oxybuprocaine hydrochloride	18F20-B02-355633	24580	40
Fagron	Oxybuprocaine hydrochloride	13J24-B07-295015	21799SI [†]	60
Fagron	Oxybuprocaine hydrochloride	15A26-B07-306787	21922SI [†]	60
Fagron	Oxybuprocaine hydrochloride	16L05-B06-334330	23719	40
Fagron	Oxybuprocaine hydrochloride	16L05-B06-334330	23720	40

- 118 902 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 7 *Apo-Ident* customers from 9 batches from the substance/substance group *Oxybuprocaine hydrochloride*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Oxybuprocaine hydrochloride	14G21B02300384	1
Fagron	Oxybuprocaine hydrochloride	12L19N01	1
Fagron	Oxybuprocaine hydrochloride	13C01-N01	4
Fagron	Oxybuprocaine hydrochloride	3613N-07321	1
Fagron	Oxybuprocaine hydrochloride	13J24B07295015	1
Fagron	Oxybuprocaine hydrochloride	15A26-B07	1
Fagron	Oxybuprocaine hydrochloride	13h13-n05	2
Fagron	Oxybuprocaine hydrochloride	4612M-03639	1
Klenk	Oxybuprocaine hydrochloride	3613M-07321	1

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Oxybuprocaine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oxybuprocaine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	235	5	118 902
Type C	0	12	1	111 234

The substance/substance group *Oxybuprocaine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	97.9167 % (> 96.6667 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Oxybuprocaine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methacholine chloride	25.53	—
Oxybutynin hydrochloride	41.36	—
Mometasone furoate, micronized	42.71	—
Dexamethasone acetate	43.69	—
Prednicarbate, micronized	45.72	—
Sildenafil citrate	45.88	—
Triamcinolone acetonide	50.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oxybuprocaine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21799	21799	0.00	40.89
20958	20958	0.00	43.69

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continued from previous page

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21922	21799	9.11	43.78
23745	20958	9.44	43.87
23752	20958	15.71	44.61

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Oxybutynin hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20565-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Oxybutynin hydrochloride; Oxybutynini hydrochloridum

Special notes

When selecting the *Oxybutynin hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5	<i>European Pharmacopoeia 9th Edition, Basic Version 2017</i> [3]
Komm2.2.40	<i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]
AA004	<i>Erstellung und Validierung eines IdentModul-Updates</i>

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Oxybutynin hydrochloride	4	3	45

Second-stage model

For differentiation of the substance/substance group *Oxybutynin hydrochloride* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oxybutynin hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Oxybutynin hydro...	13H26-B03-290572	21543	60	AR-15-FG-002173-01
Fagron	Oxybutynin hydro...	14A29-B09-293841	21704	45	20140227
Fagron	Oxybutynin hydro...	14I16-B03-312059	22732	40	20141007
Fagron	Oxybutynin hydro...	18K22-B01-359482	25059	40	20181217

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 185 spectra of 4 reference samples from the substance/substance group *Oxybutynin hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 504 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Oxybutynin hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Oxybutynin hydrochloride	12D24-N07	20565	40
Fagron	Oxybutynin hydrochloride	16A18-B02-321181	23268	40
Fagron	Oxybutynin hydrochloride	18A12-B03-344347	23995	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 104 spectra from 25 *Apo-Ident* customers from 49 batches from the substance/substance group *Oxybutynin hydrochloride*.
- Among them are spectra of independent samples from 45 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Oxybutynin hydrochloride	18A12-B03-346964	3
Audor Pharma	Oxybutynin hydrochloride	AP0H0122017201810B	2
Audor Pharma	Oxybutynin hydrochloride	AP0H/043/2017-2018	1
Audor Pharma	Oxybutynin hydrochloride	AP0H0122017-2018-10B	1
Caelo	Oxybutynin hydrochloride	15F05-B03-318524	4
Caelo	Oxybutynin hydrochloride	129099	1
Caelo	Oxybutynin hydrochloride	18A12-B03-344350	1
Caelo	Oxybutynin hydrochloride	18A12-B03-344350	1
Caelo	Oxybutynin hydrochloride	14A29-B09-307322	4
Caelo	Oxybutynin hydrochloride	16A18-B02-321181	3
Caelo	Oxybutynin hydrochloride	16A18-B02-321181	2
Caelo	Oxybutynin hydrochloride	16/23-B03-333371	3
Caelo	Oxybutynin hydrochloride	16/23-B03-328916	1
Caelo	Oxybutynin hydrochloride	16A18-B02-326183	1
Caelo	Oxybutynin hydrochloride	18A12-B03	2
Fagro/Sanacorp	Oxybutynin hydrochloride	16A18-B02-326183	1
Fagro/Sanacorp	Oxybutynin hydrochloride	16/23-B03-32891613	1
Fagron	Oxybutynin hydrochloride	13H26-B03	1
Fagron	Oxybutynin hydrochloride	13H26-B03-287325	1
Fagron	Oxybutynin hydrochloride	14/16-B03-300207	5
Fagron	Oxybutynin hydrochloride	15F05-B03-315221	6
Fagron	Oxybutynin hydrochloride	15F05-b03-315220	1
Fagron	Oxybutynin hydrochloride	1607080	1
Fagron	Oxybutynin hydrochloride	18A12-B03	1
Fagron	Oxybutynin hydrochloride	18A12-B03-347807	1
Fagron	Oxybutynin hydrochloride	18A12-B03-349624	1
Fagron	Oxybutynin hydrochloride	18K22-B01-358358	2
Fagron	Oxybutynin hydrochloride	18A12-B03-344350	1
Fagron	Oxybutynin hydrochloride	16/23-b03-333371	1
Fagron	Oxybutynin hydrochloride	18A12-B03-344347	1
Fagron	Oxybutynin hydrochloride	14I16-B03-300207	1
Fagron	Oxybutynin hydrochloride	22032F004	1
Fagron	Oxybutynin hydrochloride	14a29-b09-307322	2
Fagron	Oxybutynin hydrochloride	1709250/16I23-B03-33	1
Fagron	Oxybutynin hydrochloride	14A29-B09-307322	2

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Supplier	Substance	Batch	Spectra
Fagron	Oxybutynin hydrochloride	14/16_B03_300207	1
Fagron	Oxybutynin hydrochloride	129099	1
Fagron	Oxybutynin hydrochloride	14A29-B09-307322	1
Fagron	Oxybutynin hydrochloride	14/16-B03-300209	1
Fagron	Oxybutynin hydrochloride	14I16-B03	1
Fagron	Oxybutynin hydrochloride	16I23-B03-328916	3
Fagron	Oxybutynin hydrochloride	18A12-B03-350471	2
Fagron	Oxybutynin hydrochloride	18A12-B03-351262	1
Fagron	Oxybutynin hydrochloride	16I23-B03-333371	2
Fagron	Oxybutynin hydrochloride	16I23-b03-328916	1
Fagron	Oxybutynin hydrochloride	127979	2
Fagron	Oxybutynin hydrochloride	15F05_B03_315221	5
Fagron	Oxybutynin hydrochloride	16A18-B02-322538	3
Fagron	Oxybutynin hydrochloride	16I23-B03-329448	1
Fagron	Oxybutynin hydrochloride	16A18-B02-326183	2
Fagron	Oxybutynin hydrochloride	18A12-B03-344348	4
Noweda	Oxybutynin hydrochloride	18A12-B03-347807	1
Noweda	Oxybutynin hydrochloride	18A12-B03-351262	1
Fagron	Oxybutynin hydrochloride	15F05-B03-318524	1
Phoenix	Oxybutynin hydrochloride	16/23-B03-328916	1
Phoenix	Oxybutynin hydrochloride	22032E005	2
Phoenix	Oxybutynin hydrochloride	18A12-B03-346964	1
Phönix	Oxybutynin hydrochloride	18A12-B03-349624	1
Caelo	Oxybutynin hydrochloride	16I23-B03-328916	1
Audor Pharma	Oxybutynin hydrochloride		2

- 111 143 spectra from 742 *Apo-Ident* customers from a total of 31 843 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Oxybutynin hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oxybutynin hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	185	0	110 504
Type B	0	120	0	119 022
Type C	0	101	3	111 143

The substance/substance group *Oxybutynin hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.7568 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	97.1154 % (> 94.2308 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Oxybutynin hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mometasone furoate, micronized	24.71	—
Oxycodone hydrochloride	35.42	—
Naloxone hydrochloride dihydrate	40.47	—
Clobetasol propionate	47.92	106.88
Sildenafil citrate	48.99	—
Oxybuprocaine hydrochloride	52.93	—
⋮	⋮	⋮
Betamethasone dipropionate, micronized	>50	119.71
Beclometasone dipropionate	>50	119.75
Gentamicin sulfate	>50	255.12
Sodium citrate	>50	484.49
Sodium benzoate	>50	729.87

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oxybutynin hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21704	21543	4.07	30.33
22732	21543	3.53	32.04
25059	21543	5.00	31.36
21543	21543	0.00	31.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Oxytetracycline hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20090-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Oxytetracycline hydrochloride; Oxytetracyclini hydrochloridum

Special notes

When selecting the *Oxytetracycline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Oxytetracycline hydrochloride	12	3	125

Second-stage model

For differentiation of the substance/substance group *Oxytetracycline hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Oxytetracycline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Oxytetracycline ...	12130001	20847	60	20120530
Caelo	Oxytetracycline ...	12328103	21039	40	20121214
Caelo	Oxytetracycline ...	16077002	22503	40	AR-16-FG-011460-01
Euro OTC	Oxytetracycline ...	1306022-02	21600	60	1507542
Euro OTC	Oxytetracycline ...	1506037	21836	60	20150721*
Euro OTC	Oxytetracycline ...	1506037	21999	60	20150721*
Euro OTC	Oxytetracycline ...	1602025	22546	40	20160609*
Euro OTC	Oxytetracycline ...	1602025-01	22658	40	AR-16-FG-014422-01
Euro OTC	Oxytetracycline ...	1602025	22669	40	20160609*
Euro OTC	Oxytetracycline ...	1602025-02	22839	40	20161021
Euro OTC	Oxytetracycline ...	1602025-02	22846	40	20161021
Euro OTC	Oxytetracycline ...	1701034	23137	40	20170314*
Euro OTC	Oxytetracycline ...	1701035-02	23970	40	20170314
Fagron	Oxytetracycline ...	13D08-N11	20848	60	20110131
Fagron	Oxytetracycline ...	15D29-B99-309066	21915	60	20150522

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 720 spectra of 15 reference samples from the substance/substance group *Oxytetracycline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 109 969 spectra from a total of 1954 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Type B spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Oxytetracycline hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Oxytetracycline hydrochloride	173168	23786	40
Euro OTC	Oxytetracycline hydrochloride	1801033	23971	40
Fagron	Oxytetracycline hydrochloride	15L16-B02-322908	23226	40
Fagron	Oxytetracycline hydrochloride	15L16-B02-322908	23417	40

- 118982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 703 spectra from 275 *Apo-Ident* customers from 139 batches from the substance/substance group *Oxytetracycline hydrochloride*.
- Among them are spectra of independent samples from 125 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Oxytetracycline hydrochloride	1506037-02	31
Alliance	Oxytetracycline hydrochloride	1407012-03	1
Alliance Healthcare	Oxytetracycline hydrochloride	1205222-01	1
Alliance Healthcare	Oxytetracycline hydrochloride	1205028-02	1
Anzag	Oxytetracycline hydrochloride	12328103	1
Anzag	Oxytetracycline hydrochloride	1506037-02	1
Anzag	Oxytetracycline hydrochloride	1506037	1
Caelo	Oxytetracycline hydrochloride	163406010	1
Euro OTC	Oxytetracycline hydrochloride	1205028-01	6
Apoident	Oxytetracycline hydrochloride	1602025-01	1
Apomix/Kehr	Oxytetracycline hydrochloride	16077014	1
Apomix/Phoenix Leipzig ...	Oxytetracycline hydrochloride	1602025-02	1
Bombastus	Oxytetracycline hydrochloride	13L19-B33-290732	1
Caelo	Oxytetracycline hydrochloride	1306022-01	2
Caelo	Oxytetracycline hydrochloride	11336510	3
Caelo	Oxytetracycline hydrochloride	12G10-N04	1
Caelo	Oxytetracycline hydrochloride	21021305	1
Caelo	Oxytetracycline hydrochloride	11336507	1
Caelo	Oxytetracycline hydrochloride	5041402	1
Caelo	Oxytetracycline hydrochloride	13L19-B33	1

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Supplier	Substance	Batch	Spectra
Caelo	Oxytetracycline hydrochloride	12091405	1
Caelo	Oxytetracycline hydrochloride	1407012-01	1
Caelo	Oxytetracycline hydrochloride	14128004	1
Caelo	Oxytetracycline hydrochloride	16077003	3
Caelo	Oxytetracycline hydrochloride	16077008	6
Caelo	Oxytetracycline hydrochloride	1506037	1
Caelo	Oxytetracycline hydrochloride	16077007	2
Caelo	Oxytetracycline hydrochloride	16077011	1
Caelo	Oxytetracycline hydrochloride	16077009	1
Caelo	Oxytetracycline hydrochloride	16077016	2
Caelo	Oxytetracycline hydrochloride	16077012	1
Caelo	Oxytetracycline hydrochloride	16077017	1
Caelo	Oxytetracycline hydrochloride	16340606	3
Caelo	Oxytetracycline hydrochloride	1701034-01	1
Caelo	Oxytetracycline hydrochloride	1/01034-02	1
Caelo	Oxytetracycline hydrochloride	1701034-02	4
Caelo	Oxytetracycline hydrochloride	16340609	1
Caelo	Oxytetracycline hydrochloride	16340616	1
Caelo	Oxytetracycline hydrochloride	17316806	4
Caelo	Oxytetracycline hydrochloride	14I22-B01-301463	1
Caelo	Oxytetracycline hydrochloride	17316819	1
Caelo	Oxytetracycline hydrochloride	17316816	1
Caelo	Oxytetracycline hydrochloride	17316815	1
Caelo	Oxytetracycline hydrochloride	12328104	1
Caelo	Oxytetracycline hydrochloride	15060109	8
Caelo	Oxytetracycline hydrochloride	16077015	1
Caelo	Oxytetracycline hydrochloride	16340605	4
Caelo	Oxytetracycline hydrochloride	1602025-02	2
Caelo	Oxytetracycline hydrochloride	16077001	3
Caelo	Oxytetracycline hydrochloride	14128003	1
Caelo	Oxytetracycline hydrochloride	15060108	1
Caelo	Oxytetracycline hydrochloride	17316805	5
Caelo	Oxytetracycline hydrochloride	12328107	1
Caelo	Oxytetracycline hydrochloride	13L19-B33-290730	1
Caelo	Oxytetracycline hydrochloride	16340611	2
Caelo	Oxytetracycline hydrochloride	17316812	3
Caelo	Oxytetracycline hydrochloride	1506037-02	1
Caelo	Oxytetracycline hydrochloride	1506037-01	3
Caelo	Oxytetracycline hydrochloride	16044007	1
Caelo	Oxytetracycline hydrochloride	1607716	1
Caelo	Oxytetracycline hydrochloride	16340610	13
Fagron	Oxytetracycline hydrochloride	1801033-01	1
Caelo	Oxytetracycline hydrochloride	150603702	1
caesar	Oxytetracycline hydrochloride	16077008	2
Caesar & Loretz GmbH	Oxytetracycline hydrochloride	17316815	1
Caesar & Loretz GmbH / ...	Oxytetracycline hydrochloride	17316815	2
Caesar u. Loretz/Noweda	Oxytetracycline hydrochloride	1602025-02	1
Caesar&Loretz	Oxytetracycline hydrochloride	16340610	1
Caesar&Loretz GmbH	Oxytetracycline hydrochloride	15060109	1
EuRho	Oxytetracycline hydrochloride	1111061-01	1
EuRho	Oxytetracycline hydrochloride	1205028-01	2
Euro OTC	Oxytetracycline hydrochloride	15060109	1
Euro OTC	Oxytetracycline hydrochloride	1111061-61	1
Euro OTC	Oxytetracycline hydrochloride	1011045-01	3
Euro OTC	Oxytetracycline hydrochloride	513E-02865	1
Euro OTC	Oxytetracycline hydrochloride	120502802	2
Euro OTC	Oxytetracycline hydrochloride	1306022-01	24
Euro OTC	Oxytetracycline hydrochloride	1205028	1
Euro OTC	Oxytetracycline hydrochloride	1407012-01	15
Euro OTC	Oxytetracycline hydrochloride	28011505	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Oxytetracycline hydrochloride	15051507	1
Euro OTC	Oxytetracycline hydrochloride	1602025-1	1
Euro OTC	Oxytetracycline hydrochloride	YT160702059	2
Euro OTC	Oxytetracycline hydrochloride	1701034-015415	1
Euro OTC	Oxytetracycline hydrochloride	180103301	3
Euro OTC	Oxytetracycline hydrochloride	375-18	1
Euro OTC	Oxytetracycline hydrochloride	21111815	1
Euro OTC	Oxytetracycline hydrochloride	1111061-01	6
Euro OTC	Oxytetracycline hydrochloride	1703130H/1602025-01	1
Euro OTC	Oxytetracycline hydrochloride	1801033-02	24
Euro OTC	Oxytetracycline hydrochloride	140701203	1
Euro OTC	Oxytetracycline hydrochloride	1506037-03	18
Euro OTC	Oxytetracycline hydrochloride	1205028-02	14
Euro OTC	Oxytetracycline hydrochloride	17010301	1
Euro OTC	Oxytetracycline hydrochloride	170103402	3
Euro OTC	Oxytetracycline hydrochloride	171034-02	1
Euro OTC	Oxytetracycline hydrochloride	1801033-22	1
Euro OTC	Oxytetracycline hydrochloride	1701034-02	42
Euro OTC	Oxytetracycline hydrochloride	170034-01	1
Euro OTC	Oxytetracycline hydrochloride	1306022	1
Euro OTC	Oxytetracycline hydrochloride	1306022-03	5
Euro OTC	Oxytetracycline hydrochloride	130602202	1
Euro OTC	Oxytetracycline hydrochloride	1801033-01	56
Euro OTC	Oxytetracycline hydrochloride	1407012-02	14
Euro OTC	Oxytetracycline hydrochloride	130602201	1
Euro OTC	Oxytetracycline hydrochloride	160202502	4
Euro OTC	Oxytetracycline hydrochloride	170612181	1
Euro OTC	Oxytetracycline hydrochloride	170103401	2
Euro OTC	Oxytetracycline hydrochloride	181016183	1
Euro OTC	Oxytetracycline hydrochloride	180103302	1
Euro OTC	Oxytetracycline hydrochloride	12050-28	1
Euro OTC	Oxytetracycline hydrochloride	1407011202	1
Euro OTC	Oxytetracycline hydrochloride	16020228-02	1
Euro/ Jenne	Oxytetracycline hydrochloride	1801033-01	1
Euro/Gehe	Oxytetracycline hydrochloride	1602025-02	1
Euro/Gehe	Oxytetracycline hydrochloride	1701034-01	1
Euro/Gehe	Oxytetracycline hydrochloride	170103	1
Euro/Gehe	Oxytetracycline hydrochloride	181033-02	1
Euro OTC	Oxytetracycline hydrochloride	1701034-0104915216	1
Euro OTC	Oxytetracycline hydrochloride	150603701	1
Euro OTC	Oxytetracycline hydrochloride	1801033	3
Euro OTC	Oxytetracycline hydrochloride	15060377-01	1
Euro OTC	Oxytetracycline hydrochloride	1701034-01	42
Euro OTC	Oxytetracycline hydrochloride	1407012-03	5
Euro OTC	Oxytetracycline hydrochloride	1506037-01	27
Euro OTC	Oxytetracycline hydrochloride	YT150502056	1
Euro OTC	Oxytetracycline hydrochloride	160202501	2
Fagro/Anzag	Oxytetracycline hydrochloride	14122-B01-301464	1
Fagron	Oxytetracycline hydrochloride	14/22-B01-301464	1
Fagron	Oxytetracycline hydrochloride	12A26-N05	3
Fagron	Oxytetracycline hydrochloride	12G10-N04	7
Fagron	Oxytetracycline hydrochloride	13L19-B33-290731	2
Fagron	Oxytetracycline hydrochloride	13L19-B33	4
Fagron	Oxytetracycline hydrochloride	13I26-N11	1
Fagron	Oxytetracycline hydrochloride	14/22-B01-301465	1
Fagron	Oxytetracycline hydrochloride	14122-B01-301463	1
Fagron	Oxytetracycline hydrochloride	14I22-B01-301464	1
Fagron	Oxytetracycline hydrochloride	130602203	1
Fagron	Oxytetracycline hydrochloride	14I22-B01	1
Fagron	Oxytetracycline hydrochloride	15116-b02-322907	1

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Supplier	Substance	Batch	Spectra
Fagron	Oxytetracycline hydrochloride	1701034-02	1
Fagron	Oxytetracycline hydrochloride	15D29-B99-308608	1
Fagron	Oxytetracycline hydrochloride	15D29-B99-309067	1
Fagron	Oxytetracycline hydrochloride	912A-02865	1
Fagron	Oxytetracycline hydrochloride	15L16-B02-322908	1
Fagron	Oxytetracycline hydrochloride	15L16-B02-322907	1
Fagron	Oxytetracycline hydrochloride	14I22-B01-301465	1
Fagron	Oxytetracycline hydrochloride	4-49732A-2	1
Fagropn	Oxytetracycline hydrochloride	13L19-B33-290731	1
Fiebig	Oxytetracycline hydrochloride	1801033-01	1
Finteler Apotheke	Oxytetracycline hydrochloride	1602025-02	2
Gehe	Oxytetracycline hydrochloride	12A26-N05	2
Gehe	Oxytetracycline hydrochloride	12g10-n04	1
Gehe	Oxytetracycline hydrochloride	1205028-01	1
Gehe	Oxytetracycline hydrochloride	1306022-02	1
Gehe	Oxytetracycline hydrochloride	1602025-02	2
Gehe	Oxytetracycline hydrochloride	17316805	1
Gehe	Oxytetracycline hydrochloride	1801033-01	3
Gehe	Oxytetracycline hydrochloride	1801033-02	1
GEHE	Oxytetracycline hydrochloride	1602025-02	1
GEHE	Oxytetracycline hydrochloride	1701034-01	1
Bombastus	Oxytetracycline hydrochloride	17316812	1
Caelo	Oxytetracycline hydrochloride	17316820	2
L12	Oxytetracycline hydrochloride	12328107	1
L12	Oxytetracycline hydrochloride	16340610	1
L30	Oxytetracycline hydrochloride	1701034-02	1
Laborchemie Apolda/Phönix	Oxytetracycline hydrochloride	1506037-02	1
Nachprüfung vom 23.07.	Oxytetracycline hydrochloride	91618269	1
Norbrook Lab.Ltd.	Oxytetracycline hydrochloride	1506037-01	2
Norbrook/Gehe	Oxytetracycline hydrochloride	140701203	1
Noweda	Oxytetracycline hydrochloride	140701203	1
Noweda	Oxytetracycline hydrochloride	140701202	1
Noweda	Oxytetracycline hydrochloride	1801033-01	1
Euro OTC	Oxytetracycline hydrochloride	1407012-09	1
Phoenix	Oxytetracycline hydrochloride	3036	1
Phoenix	Oxytetracycline hydrochloride	1602025-02	1
Phoenix	Oxytetracycline hydrochloride	17316817	1
Phönix	Oxytetracycline hydrochloride	1205028-01	1
Phönix	Oxytetracycline hydrochloride	1701034-02	1
Phönix Gotha	Oxytetracycline hydrochloride	1232814	1
Phönix Gotha	Oxytetracycline hydrochloride	1407012-02	1
Sanacorp	Oxytetracycline hydrochloride	1701034-01	1
SANACORP	Oxytetracycline hydrochloride	1801033-02	1
Fagron	Oxytetracycline hydrochloride	C22H25CIN209	1
Fagron	Oxytetracycline hydrochloride	1407012-01	1
Fagron	Oxytetracycline hydrochloride	13L19-B33-290730	3
Yangzhou Liberty Pharma	Oxytetracycline hydrochloride	1801033-02	2
	Oxytetracycline hydrochloride	130602202	1
Euro OTC	Oxytetracycline hydrochloride	1306022-02	14
Caelo	Oxytetracycline hydrochloride	12130001	1
Caelo	Oxytetracycline hydrochloride	16077002	2
Caelo	Oxytetracycline hydrochloride	12328103	1
Euro OTC	Oxytetracycline hydrochloride	1602025-01	22
Euro OTC	Oxytetracycline hydrochloride	1602025-02	48
Euro OTC	Oxytetracycline hydrochloride		1
Euro OTC	Oxytetracycline hydrochloride	1602025	3
Euro OTC	Oxytetracycline hydrochloride	1506037	3
Fagron	Oxytetracycline hydrochloride	13D08-N11	6
Fagron	Oxytetracycline hydrochloride		1
	Oxytetracycline hydrochloride	1306022-02	3

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Supplier	Substance	Batch	Spectra
	Oxytetracycline hydrochloride	140701201	1
	Oxytetracycline hydrochloride		1

- 110 544 spectra from 742 *Apo-Ident* customers from a total of 31 756 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Oxytetracycline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oxytetracycline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	720	0	109 969
Type B	0	160	0	118 982
Type C	0	690	13	110 544

The substance/substance group *Oxytetracycline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.1667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	98.1508 % (> 97.7240 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Oxytetracycline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chloramphenicol	16.99	—
Sodium cromoglicate	25.07	—
Levothyroxin sodium	27.12	—
Tetracycline hydrochloride	32.95	—
Eosin Y	39.17	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Oxytetracycline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20848	22503	9.04	31.77
21039	21600	5.94	45.35
21600	21600	0.00	42.15
21836	21836	0.00	34.94
21915	22503	12.72	31.43
22839	22669	9.89	30.65
23137	23137	0.00	38.01
23970	22546	9.03	39.68
20847	21999	7.19	33.88
21999	21999	0.00	35.79
22503	22503	0.00	38.07
22546	22546	0.00	38.59
22846	22669	6.07	33.18
22658	22658	0.00	35.09
22669	22669	0.00	38.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Pancreas powder**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20976-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pancreas powder; Pancreatis pulvis

Special notes

When selecting the *Pancreas powder* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pancreas powder	4	1	0

Second-stage model

For differentiation of the substance/substance group *Pancreas powder* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pancreas powder*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Pancreas powder	13118902	20976	40	1402190
Caelo	Pancreas powder	13395203	21481	60	20131218
Caelo	Pancreas powder	161397	22482	60	20160527*
Caelo	Pancreas powder	16139708	23757	40	20160527
Caelo	Pancreas powder	16139708	23758	40	20160527

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Pancreas powder*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Pancreas powder*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Pancreas powder	173226	23797	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Pancreas powder*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pancreas powder* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pancreas powder* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Pancreas powder* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pancreas powder* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zinc gluconate	27.09	—
Neomycin sulfate	37.19	—
Aciclovir	39.04	—
Lactose monohydrate	41.29	—
Isosorbide dinitrate 40%	41.63	—
Uridine	42.05	—
Potassium sodium tartrate tetrahydrate	42.28	—
Fructose	46.83	—
SyrSpend® SF Alka	48.10	—
Levothyroxin sodium	54.84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pancreas powder* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22482	22482	0.00	38.55
20976	20976	0.00	26.41
21481	22482	9.49	34.46
23757	22482	3.04	36.08
23758	22482	3.33	35.93

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Papaverine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20481-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Papaverine hydrochloride; Papaverini hydrochloridum

Special notes

When selecting the *Papaverine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Papaverine hydrochloride	2	2	12

Second-stage model

For differentiation of the substance/substance group *Papaverine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Papaverine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Papaverine hydro...	13324310	21735	60	20130920
Caelo	Papaverine hydro...	123161	23054	40	20121127*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 100 spectra of 2 reference samples from the substance/substance group *Papaverine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 589 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Papaverine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Papaverine hydrochloride	163159	23053	40
Caelo	Papaverine hydrochloride	16315911	23928	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 14 spectra from 10 *Apo-Ident* customers from 13 batches from the substance/substance group *Papaverine hydrochloride*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Papaverine hydrochloride	12166112	1
Caelo	Papaverine hydrochloride	13324307	1
Caelo	Papaverine hydrochloride	12166105	1
Caelo	Papaverine hydrochloride	16315911	1
Caelo	Papaverine hydrochloride	16315907	1
Caelo	Papaverine hydrochloride	17358802	1
Caelo	Papaverine hydrochloride	12316105	1
Caelo	Papaverine hydrochloride	15160608	2
Caelo	Papaverine hydrochloride	16315903	1
GATT-KOLLER/PHOENIX	Papaverine hydrochloride	2927/07131314	1
Phönix Gotha	Papaverine hydrochloride	12166101	1
Phönix Gotha	Papaverine hydrochloride	13324306	1
Caelo	Papaverine hydrochloride		1

- 111 233 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Papaverine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Papaverine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	110 589
Type B	0	80	0	119 062
Type C	0	13	1	111 233

The substance/substance group *Papaverine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Papaverine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Methadone hydrochloride	29.43	—
Diltiazem hydrochloride	32.21	—
Doxylamine hydrogen succinate	42.55	—
Cocaine hydrochloride	48.13	—
Ethyl hydrogen fumarate calcium	63.08	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Papaverine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21735	23054	11.36	46.55
23054	23054	0.00	46.06

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Paracetamol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20972-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Paracetamol; Paracetamolum

Special notes

When selecting the *Paracetamol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Paracetamol	7	2	29

Second-stage model

For differentiation of the substance/substance group *Paracetamol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Paracetamol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Paracetamol	15075706	22608	40	20150424
Caelo	Paracetamol	15075707	22822	40	20150424
Caelo	Paracetamol	191851	24889	40	20190827*
Euro OTC	Paracetamol	1111024-02	21598	60	20120123
Fagron	Paracetamol	13D30-N03	20972	40	1402271
Fagron	Paracetamol	13D16-N08	20973	40	1402296
Fagron	Paracetamol	13G23-N03	20974	40	1402297

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 7 reference samples from the substance/substance group *Paracetamol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 389 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Paracetamol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Paracetamol	170284	23852	40
Caelo	Paracetamol	180830	24053	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 47 spectra from 22 *Apo-Ident* customers from 30 batches from the substance/substance group *Paracetamol*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Paracetamol	11300108	1
Caelo	Paracetamol	11300120	2
Caelo	Paracetamol	13082010	2
Caelo	Paracetamol	15217704	1
Caelo	Paracetamol	15217710	3
Caelo	Paracetamol	18083005	4
Caelo	Paracetamol	18083006	1
Caelo	Paracetamol	15217712	1
Caelo	Paracetamol	10325020	1
Caelo	Paracetamol	13082005	1
Caelo	Paracetamol	15245902	1
Caelo	Paracetamol	15217708	1
Caelo	Paracetamol	13082011	1
Caelo	Paracetamol	18083014	1
Caelo	Paracetamol	15075704	4
Caelo	Paracetamol	15075708	1
Caelo	Paracetamol	1912M-02045	1
Caelo	Paracetamol	1814U-02045	1
Caelo	Paracetamol	2815I-02045	1
Caelo	Paracetamol	17028411	2
Caelo	Paracetamol	18083003	1
Caelo	Paracetamol	15217706	1
Caelo	Paracetamol	15217701	1
Caelo	Paracetamol	17028409	3
Caesar & Loretz GmbH	Paracetamol	18083006	1
Caesar & Loretz GmbH	Paracetamol	18083008	1
Euro OTC	Paracetamol	17028409	1
Euro OTC	Paracetamol	1111024-01	1
Fagron	Paracetamol	13L16-B02-322725	1
Caelo	Paracetamol	10065102	1
Jenne	Paracetamol	15245901	1
Nachprüfung	Paracetamol	15245901	2
Euro OTC	Paracetamol	1111024-02	1

- 111 200 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Paracetamol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Paracetamol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	80	0	119 062
Type C	0	46	1	111 200

The substance/substance group *Paracetamol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	97.8723 % (> 91.4894 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Paracetamol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sulfogaiacol hydrate	29.16	—
Sodium cromoglicate	37.11	—
Griffonia seed extract	40.61	—
Serine	43.21	—
Vanillin	48.90	—
Choline hydrogen tartrate	58.02	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Paracetamol* is separated from critical neighbours in a second-stage model,

all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22608	24889	3.05	40.61
20972	20972	0.00	42.32
20973	20973	0.00	42.67
21598	24889	3.45	41.30
22822	24889	3.52	43.09
24889	24889	0.00	40.75
20974	20974	0.00	52.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Patent blue V**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20469-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Patent blue V

Special notes

When selecting the *Patent blue V* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Patent blue V	4	1	11

Second-stage model

For differentiation of the substance/substance group *Patent blue V* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Patent blue V*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Patent blue V	12364206	21384	40	1508043
Caelo	Patent blue V	12364206	21385	40	20130110
Caelo	Patent blue V	13351803	21695	60	20131114
Caelo	Patent blue V	13351807	22387	40	1702362
Caelo	Patent blue V	190746	24731	40	20190425*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Patent blue V*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Patent blue V*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Patent blue V	16306902	23214	40
Caelo	Patent blue V	16306902	23215	40

- 119 062 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 32 spectra from 31 *Apo-Ident* customers from 14 batches from the substance/substance group *Patent blue V*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Patent blue V	11305302	1
Bombastus	Patent blue V	17034204	1
Caelo	Patent blue V	2759	1
Caelo	Patent blue V	11305303	3
Caelo	Patent blue V	12364202	1
Caelo	Patent blue V	15060204	1
Caelo	Patent blue V	11305302	1
Caelo	Patent blue V	13351808	1
Caelo	Patent blue V	17034207	3
Caelo	Patent blue V	17034204	5
Caelo	Patent blue V	150602	1
GEHE	Patent blue V	17034207	1
Caelo	Patent blue V	16306904	1
Euro OTC	Patent blue V	17034210	1
Caelo	Patent blue V	12364206	4
Caelo	Patent blue V	13351803	1
Caelo	Patent blue V	13351807	5

- 111 215 spectra from 742 *Apo-Ident* customers from a total of 31 877 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Patent blue V* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Patent blue V* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	51	29	119 062
Type C	0	27	5	111 215

The substance/substance group *Patent blue V* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	63.7500 % (> 60.0000 %)
Type C	100.0000 % (> 99.8899 %)	84.3750 % (> 75.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Patent blue V* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Eosin Y	72.07	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Patent blue V* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24731	24731	0.00	82.27
21384	21384	0.00	77.58
21385	21384	1.92	77.51
21695	22387	2.54	84.64
22387	22387	0.00	84.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Phenazone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22532-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Phenazone; Phenazonum

Special notes

When selecting the *Phenazone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Phenazone	5	2	1

Second-stage model

For differentiation of the substance/substance group *Phenazone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Phenazone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Phenazone	15415101	22576	40	20151215
Caelo	Phenazone	15415107	22827	40	20151215
Caelo	Phenazone	181347	24259	40	20180629*
Fagron	Phenazone	13G16-B07-287172	22532	40	AR-16-FG-011360-01
Fagron	Phenazone	13G16-B07-287172	22720	40	20130814
Fagron	Phenazone	15H28-B09-322944	24698	40	20150916

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Phenazone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Phenazone*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Phenazone	170836	23302	40
Caelo	Phenazone	182565	24369	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Phenazone*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Phenazone	18061101	1

- 111 246 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Phenazone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenazone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	1	0	111 246

The substance/substance group *Phenazone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8911 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Phenazone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Caffeine	34.37	–
L-tryptophan	46.52	–
Midazolam hydrochloride	46.59	–
Ethyl hydrogen fumarate calcium	51.15	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Phenazone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22720	22532	1.33	41.99
22532	22532	0.00	41.54
24698	22532	10.48	47.02
22576	24259	5.32	43.95
22827	24259	7.19	45.08
24259	24259	0.00	42.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Pheniramine maleate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20694-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pheniramine maleate; Pheniramini maleas

Special notes

When selecting the *Pheniramine maleate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pheniramine maleate	5	3	26

Second-stage model

For differentiation of the substance/substance group *Pheniramine maleate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pheniramine maleate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Pheniramine male...	12200502	20694	40	1401559
Caelo	Pheniramine male...	15172702	22790	40	1908273
Euro OTC	Pheniramine male...	1910024	24921	40	20191122*
Fagron	Pheniramine male...	13D24-N04	20928	40	20130530
Fagron	Pheniramine male...	18C21-B02-362029	24948	40	20180426

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Pheniramine maleate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 489 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Pheniramine maleate*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Pheniramine maleate	173167	23821	40
Euro OTC	Pheniramine maleate	1109013-02	20756	40
Euro OTC	Pheniramine maleate	1701021	23384	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 53 spectra from 30 *Apo-Ident* customers from 27 batches from the substance/substance group *Pheniramine maleate*.
- Among them are spectra of independent samples from 26 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance Healthcare	Pheniramine maleate	12L04-N05	1
Caelo	Pheniramine maleate	12352604	1
Caelo	Pheniramine maleate	14C25-B01-302272	1
Caelo	Pheniramine maleate	1235611	1
Caelo	Pheniramine maleate	17316702	1
Caelo	Pheniramine maleate	15172708	1
Caelo	Pheniramine maleate	9276210	1
Caelo	Pheniramine maleate	15172704	1
Caelo	Pheniramine maleate	12352602	1
Caelo	Pheniramine maleate	14C25-B01-322989	1
Caelo	Pheniramine maleate	15172711	1
Cealo	Pheniramine maleate	12352608	1
EuRO 14.11.2013 Phönix	Pheniramine maleate	1209032-01	1
Euro OTC	Pheniramine maleate	1209032-01	2
Euro OTC	Pheniramine maleate	1411044-01	1
Euro OTC	Pheniramine maleate	1701021-01	7
Euro OTC	Pheniramine maleate	1109013-01	1
Euro OTC	Pheniramine maleate	1411044-02	3
Fagron	Pheniramine maleate	12L04-N05	3
Fagron	Pheniramine maleate	14C25-B01-292540	1
Fagron	Pheniramine maleate	14C25-B01-307150	3
Fagron	Pheniramine maleate	14c25-b01-307150	1
Fagron	Pheniramine maleate	14c25b01307150	1
Fagron	Pheniramine maleate	12I06-N02	1
Fagron	Pheniramine maleate	14C25-B01-328732	2
Fagron	Pheniramine maleate	14C25-B01-295293	3
Noweda 28.08.2019	Pheniramine maleate	15172714	1
Caelo	Pheniramine maleate	14C25-B01-292540	1
Spangro_07.11.2018	Pheniramine maleate	1701021-01	7
Supriya LifeScience Ltd...	Pheniramine maleate	SLL/P/1213063	1
Supriya LifeScience Ltd...	Pheniramine maleate	14C25-B01	1

- 111 194 spectra from 742 *Apo-Ident* customers from a total of 31 864 batches from a further 706

substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pheniramine maleate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pheniramine maleate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	120	0	119 022
Type C	0	53	0	111 194

The substance/substance group *Pheniramine maleate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 88.6792 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pheniramine maleate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-tryptophan	25.97	—
Dithranol	53.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pheniramine maleate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20694	20694	0.00	23.50
20928	24921	4.99	23.07
22790	22790	0.00	24.52
24921	24921	0.00	25.46
24948	24921	10.82	27.38

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Phenylbutazon**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20447-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Phenylbutazon; Phenylbutazonum

Special notes

When selecting the *Phenylbutazon* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Phenylbutazon	5	3	7

Second-stage model

For differentiation of the substance/substance group *Phenylbutazon* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Phenylbutazon*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Phenylbutazon	14057202	21379	40	20140321
Caelo	Phenylbutazon	161121	22471	60	20160331*
Euro OTC	Phenylbutazon	1305050-02	21605	60	AR-15-FG-005687-01
Euro OTC	Phenylbutazon	1507023	21855	60	20150805*
Euro OTC	Phenylbutazon	1908013	24861	40	20190923*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *Phenylbutazon*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Phenylbutazon*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Phenylbutazon	1604033	22563	40
Euro OTC	Phenylbutazon	1804018	24122	40
Fagron	Phenylbutazon	18B21-B06-361114	24952	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 7 spectra from 7 *Apo-Ident* customers from 7 batches from the substance/substance group *Phenylbutazon*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Phenylbutazon	10262901	1
Caelo	Phenylbutazon	15218502	1
Euro OTC	Phenylbutazon	180401802	1
Euro OTC	Phenylbutazon	170612PB/1604033-01	1
Euro OTC	Phenylbutazon	19091806	1
Fagron	Phenylbutazon	11H26-N02	1
Fagron	Phenylbutazon	13D30-N16	1

- 111 240 spectra from 742 *Apo-Ident* customers from a total of 31 884 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Phenylbutazon* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenylbutazon* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	120	0	119 022
Type C	0	7	0	111 240

The substance/substance group *Phenylbutazon* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Phenylbutazon* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Indometacin	32.16	—
Thalidomide	35.44	—
L-tryptophan	50.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Phenylbutazon* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21379	21605	3.34	32.40
21605	21605	0.00	32.71
21855	21855	0.00	32.02
22471	22471	0.00	32.20
24861	24861	0.00	32.43

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Phenylephrine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20567-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Phenylephrine hydrochloride; Phenylephrini hydrochloridum

Special notes

When selecting the *Phenylephrine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Phenylephrine hydrochloride	5	2	42

Second-stage model

For differentiation of the substance/substance group *Phenylephrine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Phenylephrine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Phenylephrine hy...	1704009	23394	40	20170524*
Euro OTC	Phenylephrine hy...	2001012	25102	40	20200218*
Fagron	Phenylephrine hy...	12J19-B40-288254	21051	40	20131210
Fagron	Phenylephrine hy...	14H13-B02-308438	21960	60	AR-16-FG-008920-01
Fagron	Phenylephrine hy...	16A20-B07-317987	22388	40	AR-16-FG-013385-01

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Phenylephrine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Phenylephrine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Phenylephrine hydrochloride	17C23-B04-333878	23263	40
Fagron	Phenylephrine hydrochloride	17C23-B04-333880	23267	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 77 spectra from 18 *Apo-Ident* customers from 46 batches from the substance/substance group *Phenylephrine hydrochloride*.
- Among them are spectra of independent samples from 42 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ALH	Phenylephrine hydrochloride	16A20-B07-322159	1
Fagron	Phenylephrine hydrochloride	17C23-B04-334819	3
Caelo	Phenylephrine hydrochloride	14H13-B02-308438	1
Caelo	Phenylephrine hydrochloride	17C23-B04-334819	1
Caelo	Phenylephrine hydrochloride	17H18-B02-353092	1
Fagron	Phenylephrine hydrochloride	12C08-N17	1
Fagron	Phenylephrine hydrochloride	13A03-N09	3
Fagron	Phenylephrine hydrochloride	12A03-N09	1
Fagron	Phenylephrine hydrochloride	12G19-N04	1
Fagron	Phenylephrine hydrochloride	1021402	1
Fagron	Phenylephrine hydrochloride	14H13B02-299817	1
Fagron	Phenylephrine hydrochloride	14H13B02299817	1
Fagron	Phenylephrine hydrochloride	14H13-B02-299814	1
Fagron	Phenylephrine hydrochloride	10091504	1
Fagron	Phenylephrine hydrochloride	16A-B07-317987	1
Fagron	Phenylephrine hydrochloride	17C23-B04-333878	3
Fagron	Phenylephrine hydrochloride	12031801	1
Fagron	Phenylephrine hydrochloride	2-IL-D-0080117	1
Fagron	Phenylephrine hydrochloride	17-H18-B02	1
Fagron	Phenylephrine hydrochloride	17-H18-B02-353092	1
Fagron	Phenylephrine hydrochloride	18L06-B02-360768	1
Fagron	Phenylephrine hydrochloride	12g19-n04	1
Fagron	Phenylephrine hydrochloride	15F09-B08-316796	1
Fagron	Phenylephrine hydrochloride	16A20-B07-323398	3
Fagron	Phenylephrine hydrochloride	17H18-B02-349261	1
Fagron	Phenylephrine hydrochloride	13G10-N04	1
Fagron	Phenylephrine hydrochloride	14H13-B02-299816	2
Fagron	Phenylephrine hydrochloride	17H18-B02-345401	2
Fagron	Phenylephrine hydrochloride	13B14-N03	1
Fagron	Phenylephrine hydrochloride	13K25-B02-293844	3
Fagron	Phenylephrine hydrochloride	13K25-B02-293845	1
Fagron	Phenylephrine hydrochloride	14H13-B02-309892	3
Fagron	Phenylephrine hydrochloride	17C23-B04-333880	1
Gatt-Koller	Phenylephrine hydrochloride	330010164116	1
GEHE	Phenylephrine hydrochloride	17H18-B02-345401	2
GEHE	Phenylephrine hydrochloride	17H18-B02	6

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Supplier	Substance	Batch	Spectra
GEHE	Phenylephrine hydrochloride	18L06-B02	3
Jenne	Phenylephrine hydrochloride	14H13-B02	2
JENNE	Phenylephrine hydrochloride	17H18-B02-339756	1
Noweda	Phenylephrine hydrochloride	12F01-N20	2
Noweda/Fargon	Phenylephrine hydrochloride	17C23-B04-336301	4
Phoenix	Phenylephrine hydrochloride	15F09-B08	1
PHÖNIX	Phenylephrine hydrochloride	17C23-B04-334819	1
Fargon	Phenylephrine hydrochloride	17c23-b04-333880	1
Fargon	Phenylephrine hydrochloride	12J19-B40-288253	2
Fargon	Phenylephrine hydrochloride	PEH-170717	1
Fargon	Phenylephrine hydrochloride	17H-18-B02-353092	1
Fargon	Phenylephrine hydrochloride	16A20-B07-317987	2

- 111 170 spectra from 742 *Apo-Ident* customers from a total of 31 846 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Phenylephrine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenylephrine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	80	0	119 062
Type C	0	76	1	111 170

The substance/substance group *Phenylephrine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	98.7013 % (> 94.8052 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Phenylephrine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Thalidomide	42.77	—
Ciprofloxacin hydrochloride	45.77	—
Midazolam hydrochloride	47.65	—
Dequalinium chloride	49.34	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Phenylephrine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22388	22388	0.00	51.20
21051	21960	2.23	55.00
21960	21960	0.00	54.49
23394	23394	0.00	51.93
25102	25102	0.00	48.79

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Phenytoin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20949-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Phenytoin; Phenytoinum

Special notes

When selecting the *Phenytoin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Phenytoin	4	3	3

Second-stage model

For differentiation of the substance/substance group *Phenytoin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Phenytoin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Phenytoin	13G26-N02	20949	40	1401380
Fagron	Phenytoin	15E12-B05-312661	22271	45	20150519
Fagron	Phenytoin	18F01-B02-350492	24438	40	20180705
Fagron	Phenytoin	18F01-B02-350492	24693	40	20180705
Fagron	Phenytoin	19E14-B02	24818	40	20190722

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 205 spectra of 5 reference samples from the substance/substance group *Phenytoin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 484 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Phenytoin*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Phenytoin	12I07-N02	20678	40
Fagron	Phenytoin	16C14-B06-325086	23110	40
Fagron	Phenytoin	17L22-B04-345861	23994	40
Fagron	Phenytoin	16C14-B06-325086	23377	40

- 118982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 3 *Apo-Ident* customers from 4 batches from the substance/substance group *Phenytoin*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Phenytoin	17L22-B04-345861	1
Fagron	Phenytoin	12C27N13	1
Fagron	Phenytoin	12I07-N02	1
Fagron	Phenytoin	13G26-N02	1

- 111243 spectra from 742 *Apo-Ident* customers from a total of 31887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Phenytoin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Phenytoin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	205	0	110484
Type B	0	160	0	118982
Type C	0	4	0	111243

The substance/substance group *Phenytoin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0732 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Phenytoin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	42.26	—
Ciprofloxacin hydrochloride	59.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Phenytoin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20949	20949	0.00	78.99
22271	20949	12.22	81.19
24438	20949	4.93	79.45
24693	20949	2.93	80.01
24818	20949	4.82	79.88

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Pilocarpine hydrochloride
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	21519-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Pilocarpine hydrochloride; Pilocarpini hydrochloridum

Special notes

When selecting the *Pilocarpine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pilocarpine hydrochloride	6	3	22

Second-stage model

For differentiation of the substance/substance group *Pilocarpine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pilocarpine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Pilocarpine hydr...	12217319	21518	60	20120806
Caelo	Pilocarpine hydr...	12217319	21519	60	1501660
Caelo	Pilocarpine hydr...	171595	23337	40	20170606*
Caelo	Pilocarpine hydr...	17124208	23371	40	20170607
Euro OTC	Pilocarpine hydr...	1305044-01	21629	60	20130725
Euro OTC	Pilocarpine hydr...	1305044-01	21629SI	60	20130725
Euro OTC	Pilocarpine hydr...	1603047	22553	40	20160429*
Euro OTC	Pilocarpine hydr...	1603047	22553SI	40	20160429*
Euro OTC	Pilocarpine hydr...	1908008	24845	40	20190830*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 9 reference samples from the substance/substance group *Pilocarpine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 249 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 420 spectra of 10 reference samples from the substance/substance group *Pilocarpine hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Pilocarpine hydrochloride	171242	23338	40
Caelo	Pilocarpine hydrochloride	191220	24762	40
Euro OTC	Pilocarpine hydrochloride	1806012	24140	40
Caelo	Pilocarpine hydrochloride	12217319	21518SI [†]	60
Caelo	Pilocarpine hydrochloride	171595	23337SI [†]	40
Caelo	Pilocarpine hydrochloride	171242	23338SI	40
Caelo	Pilocarpine hydrochloride	17124208	23371SI [†]	40
Caelo	Pilocarpine hydrochloride	191220	24762SI	40
Euro OTC	Pilocarpine hydrochloride	1806012	24140SI	40
Euro OTC	Pilocarpine hydrochloride	1908008	24845SI [†]	40

- 118 722 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 72 spectra from 51 *Apo-Ident* customers from 25 batches from the substance/substance group *Pilocarpine hydrochloride*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Pilocarpine hydrochloride	2211112032607	1
Caelo	Pilocarpine hydrochloride	25051303	1
Caelo	Pilocarpine hydrochloride	12217302	1
Caelo	Pilocarpine hydrochloride	12217307	1
Caelo	Pilocarpine hydrochloride	12217316	1
Caelo	Pilocarpine hydrochloride	130504401	1
Caelo	Pilocarpine hydrochloride	15198610	1
Caelo	Pilocarpine hydrochloride	17236401	1
Caelo	Pilocarpine hydrochloride	1603047-02	2
Caelo	Pilocarpine hydrochloride	18138704	2
Caelo	Pilocarpine hydrochloride	12K07-N09	1
Euro OTC	Pilocarpine hydrochloride	130504401	2
Euro OTC	Pilocarpine hydrochloride	13050-14-01	1
Euro OTC	Pilocarpine hydrochloride	1202031-01	1
Euro OTC	Pilocarpine hydrochloride	1202031-02	1
Euro OTC	Pilocarpine hydrochloride	Euroo	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Euro OTC	Pilocarpine hydrochloride	1806012-01	4
Euro OTC	Pilocarpine hydrochloride	1603047-01	5
Euro OTC	Pilocarpine hydrochloride	1603047-02	23
Euro OTC	Pilocarpine hydrochloride	160304702	1
Euro OTG	Pilocarpine hydrochloride	1305044-01	1
Euro OTC	Pilocarpine hydrochloride	1305044-03	2
Fagron	Pilocarpine hydrochloride	13H24-N03	1
Fagron	Pilocarpine hydrochloride	15B27-B03-309493	1
Gehe	Pilocarpine hydrochloride	15198610	1
GEHE	Pilocarpine hydrochloride	18138704	1
Phönix	Pilocarpine hydrochloride	1603047-02	1
Caelo	Pilocarpine hydrochloride	1305044-03	1
Sanacorp	Pilocarpine hydrochloride	12217302	1
Euro OTC	Pilocarpine hydrochloride	1806012-02	1
Caelo	Pilocarpine hydrochloride	17124208	3
Euro OTC	Pilocarpine hydrochloride	1305044-01	5
Euro OTC	Pilocarpine hydrochloride	1603047	1

- 111 175 spectra from 742 *Apo-Ident* customers from a total of 31 866 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pilocarpine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pilocarpine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	110 249
Type B	0	420	0	118 722
Type C	0	72	0	111 175

The substance/substance group *Pilocarpine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.5714 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 91.6667 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pilocarpine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ofloxacin	29.27	—
Tretinoin	50.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pilocarpine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21518	21519	6.67	35.40
21519	21519	0.00	33.91
21629	24845	2.88	35.11
22553	22553	0.00	34.24
23337	23337	0.00	33.40
23371	22553	3.90	35.19
24845	24845	0.00	34.42

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Poloxamers 407**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20540-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Poloxamers 407; Poloxamera

Special notes

When selecting the *Poloxamers 407* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Poloxamers 407	3	4	35

Second-stage model

For differentiation of the substance/substance group *Poloxamers 407* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Poloxamers 407*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Poloxamers 407	14196101	21652	60	AR-14-FG-013090-01
Caelo	Poloxamers 407	16242605	23257	40	20160915
Fagron	Poloxamers 407	14G17-B03-296866	21726	60	20140806

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Poloxamers 407*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Poloxamers 407*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Poloxamers 407	170486	23311	40
Caelo	Poloxamers 407	172921	23810	40
Caelo	Poloxamers 407	181607	24219	40
Caelo	Poloxamers 407	182636	24358	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 77 spectra from 48 *Apo-Ident* customers from 37 batches from the substance/substance group *Poloxamers 407*.
- Among them are spectra of independent samples from 35 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Poloxamers 407	12286801	2
Caelo	Poloxamers 407	14196108	2
Caelo	Poloxamers 407	14196105	1
Caelo	Poloxamers 407	14359501	1
Caelo	Poloxamers 407	14196104	1
Caelo	Poloxamers 407	16189302	4
Caelo	Poloxamers 407	16242601	3
Caelo	Poloxamers 407	16189301	1
Caelo	Poloxamers 407	17292101	2
Caelo	Poloxamers 407	18025101	10
Caelo	Poloxamers 407	18160702	3
Caelo	Poloxamers 407	18263601	2
Caelo	Poloxamers 407	18263605	2
Caelo	Poloxamers 407	17048601	4
Caelo	Poloxamers 407	17048606	2
Caelo	Poloxamers 407	12286805	1
Caelo	Poloxamers 407	15397802	5
Caelo	Poloxamers 407	12286806	1
Caelo	Poloxamers 407	13133203	2
Caelo	Poloxamers 407	18263607	1
Caelo	Poloxamers 407	13133201	1
Caelo	Poloxamers 407	13133207	1
Caesar & Loretz GmbH	Poloxamers 407	15183102	1
Caesar & Loretz GmbH	Poloxamers 407	18263607	1
Euro OTC	Poloxamers 407	15397802	1
Fagron	Poloxamers 407	12K23-N03	1
Fagron	Poloxamers 407	5211Q-07027	1
Fagron	Poloxamers 407	WPWI610C	1
Fagron	Poloxamers 407	15A26-B03-303503	1
Fagron	Poloxamers 407	315E-07027	1
Fagron	Poloxamers 407	5315I-07027	1
Fagron	Poloxamers 407	13G29-N01	1
Fagron	Poloxamers 407	13G29-N01	1
Fagron	Poloxamers 407	914I-07027	1
Caelo	Poloxamers 407	162426056	1
Caelo	Poloxamers 407	15183102	2
Caelo	Poloxamers 407	18160704	3
Phonix	Poloxamers 407	12/13-N10	1
Sanacorp	Poloxamers 407	14196101	2
Caelo	Poloxamers 407	14196101	2
Caelo	Poloxamers 407	16242605	2

- 111 170 spectra from 742 *Apo-Ident* customers from a total of 31 854 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Poloxamers 407* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Poloxamers 407* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	160	0	118 982
Type C	0	69	8	111 170

The substance/substance group *Poloxamers 407* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	89.6104 % (> 85.7143 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Poloxamers 407* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hard fat in pastilles	27.98	—
Cocoa butter	28.52	—
Magnesium stearate	35.61	—
Wax, bleached	39.70	—
Cetyl palmitate 15	42.97	—
Hard fat W35	45.41	—
Wax, yellow	47.95	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Poloxamers 407* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21652	21652	0.00	31.85
21726	21652	4.65	31.48
23257	21652	2.90	32.27

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Polymyxin B sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20853-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Polymyxin B sulfate; Polymyxin B sulphate; Polymyxini B sulfas

Special notes

When selecting the *Polymyxin B sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Polymyxin B sulfate	12	9	42

Second-stage model

For differentiation of the substance/substance group *Polymyxin B sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Polymyxin B sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Polymyxin B sulf. . .	153501	22451	60	20160318*
Caelo	Polymyxin B sulf. . .	181154	24407	40	20180507*
Euro OTC	Polymyxin B sulf. . .	1304033-01	21094	40	20130829
Euro OTC	Polymyxin B sulf. . .	1202039-02	21329	40	1411033
Euro OTC	Polymyxin B sulf. . .	1304033-02	21584	60	20130612
Euro OTC	Polymyxin B sulf. . .	1505005-01	21980	60	AR-16-FG-005387-01
Euro OTC	Polymyxin B sulf. . .	1604016	22542	40	20160509*
Fagron	Polymyxin B sulf. . .	13C12-N02	20853	40	1402691
Fagron	Polymyxin B sulf. . .	12G13-N05	21258	40	1410347
Fagron	Polymyxin B sulf. . .	13I13-N05	21595	45	AR-15-FG-001516-01
Fagron	Polymyxin B sulf. . .	14F04-B03-296722	21957	60	20140708
Fagron	Polymyxin B sulf. . .	15H14-B01-314364	22323	60	20150902

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 585 spectra of 12 reference samples from the substance/substance group *Polymyxin B sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 110 104 spectra from a total of 1954 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 400 spectra of 10 reference samples from the substance/substance group *Polymyxin B sulfate*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Polymyxin B sulfate	191131	24752	40
Euro OTC	Polymyxin B sulfate	1701010	23012	40
Euro OTC	Polymyxin B sulfate	1707013	23554	40
Euro OTC	Polymyxin B sulfate	1802006	23953	40
Euro OTC	Polymyxin B sulfate	1807004	24143	40
Euro OTC	Polymyxin B sulfate	1811022	24494	40
Euro OTC	Polymyxin B sulfate	1906002	24779	40
Euro OTC	Polymyxin B sulfate	1911021	25088	40
Fagron	Polymyxin B sulfate	13E06-N12	20912	40
Euro OTC	Polymyxin B sulfate	1202039-02	20904	40

- 118 742 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 118 spectra from 85 *Apo-Ident* customers from 48 batches from the substance/substance group *Polymyxin B sulfate*.
- Among them are spectra of independent samples from 42 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance Healthcare	Polymyxin B sulfate	1202039-02	1
Bombastus	Polymyxin B sulfate	1604016-02	1
Caelo	Polymyxin B sulfate	13H28-B02-287953	1
Caelo	Polymyxin B sulfate	1604016-01	3
Caelo	Polymyxin B sulfate	1701010-01	1
Caelo	Polymyxin B sulfate	170101001	3
Caelo	Polymyxin B sulfate	150725	1
Caelo	Polymyxin B sulfate	1707013-01	1
Caelo	Polymyxin B sulfate	15350101	6
Caelo	Polymyxin B sulfate	1802006-011	1
Caelo	Polymyxin B sulfate	1102013-01	1
Caelo	Polymyxin B sulfate	1802006-01	2
cealo	Polymyxin B sulfate	16c01-b04-319432	1
EuRho	Polymyxin B sulfate	1202039-01	1
Euro OTC	Polymyxin B sulfate	25101201	1
Euro OTC	Polymyxin B sulfate	11091419	1
Euro OTC	Polymyxin B sulfate	23051502	1
Euro OTC	Polymyxin B sulfate	1505505-01	1
Euro OTC	Polymyxin B sulfate	1701010-01	11

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Supplier	Substance	Batch	Spectra
Euro OTC	Polymyxin B sulfate	1802006-01	4
Euro OTC	Polymyxin B sulfate	28041730	1
Euro OTC	Polymyxin B sulfate	1406012-01	3
Euro OTC	Polymyxin B sulfate	1707013-01	8
Euro OTC	Polymyxin B sulfate	170101001	1
Euro OTC	Polymyxin B sulfate	1604016-01	1
Euro OTC	Polymyxin B sulfate	180200601	1
Euro OTC	Polymyxin B sulfate	1807004-01	1
Euro OTC	Polymyxin B sulfate	140601202	3
Euro/Phoenix	Polymyxin B sulfate	1304033-02	1
Euro OTC	Polymyxin B sulfate	1202039-01	1
Euro OTC	Polymyxin B sulfate	1406012-02	5
Euro OTC	Polymyxin B sulfate	1304033-03	2
Euro OTC	Polymyxin B sulfate	150500501	1
Euro OTC	Polymyxin B sulfate	1604016-02	3
Euro OTC	Polymyxin B sulfate	1811022-01	3
Fagron	Polymyxin B sulfate	17H23-B01-344840	1
Fagron	Polymyxin B sulfate	13G05-N06	2
Fagron	Polymyxin B sulfate	13H28-B02-287954	1
Fagron	Polymyxin B sulfate	14F04-B03-296721	1
Fagron	Polymyxin B sulfate	14H12-B06-304727	1
Fagron	Polymyxin B sulfate	16G21-B03-333808	1
Fagron	Polymyxin B sulfate	16C01-B04	1
Fagron	Polymyxin B sulfate	16C01-B04-322012	3
Fagron	Polymyxin B sulfate	15H14-B01-315692	1
Fagron	Polymyxin B sulfate	13/13-N05	1
Fagron	Polymyxin B sulfate	13H28-B02-293470	1
Fagron	Polymyxin B sulfate	912A-03315	1
Fiebig	Polymyxin B sulfate	1807004-01	1
Gatt-Koller	Polymyxin B sulfate	17H23B01344840	1
Gehe	Polymyxin B sulfate	170101001	1
GEHE	Polymyxin B sulfate	1701010-01	1
Noweda 03.08.2019	Polymyxin B sulfate	18115406	1
Phoenix	Polymyxin B sulfate	1807004-01	1
Phönix	Polymyxin B sulfate	1202039-01	1
Phönix	Polymyxin B sulfate	1701010-01	1
Caelo	Polymyxin B sulfate	16C01-B04-319432	1
Phönix/Euro	Polymyxin B sulfate	1505005-010	1
Rondell Apotheke	Polymyxin B sulfate	121161	1
Sanacorp	Polymyxin B sulfate	1707013-01	1
Euro OTC	Polymyxin B sulfate	1202039-02	4
Euro OTC	Polymyxin B sulfate	1505005-01	6
Euro OTC	Polymyxin B sulfate	1304033-02	1
Fagron	Polymyxin B sulfate	12G13-N05	1
Euro OTC	Polymyxin B sulfate	1304033-01	1

- 111 129 spectra from 742 *Apo-Ident* customers from a total of 31 844 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Polymyxin B sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Polymyxin B sulfate* and it was

evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	584	1	110 104
Type B	0	360	40	118 742
Type C	0	110	8	111 129

The substance/substance group *Polymyxin B sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	99.8291 % (> 99.3162 %)
Type B	100.0000 % (> 99.9893 %)	90.0000 % (> 89.2500 %)
Type C	100.0000 % (> 99.8899 %)	93.2203 % (> 90.6780 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Polymyxin B sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium citrate	13.50	—
Triamcinolone, micronized	23.34	—
Bacitracin	25.58	—
Riboflavin	27.51	—
Colistin sulfate	29.56	—
Citrulline	29.72	—
Prednisone	29.86	—
Riboflavin phosphate sodium	30.21	—
Clindamycin hydrochloride	32.49	—
Calcium pantothenate	33.87	—
Estradiol hemihydrate	35.20	—
Levothyroxin sodium	36.88	—
Minoxidil	37.30	—
Calcium citrate tetrahydrate	40.81	—
Thiamine chloride hydrochloride	43.85	—
Cyanocobalamin	45.95	—
Nystatin	46.09	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Polymyxin B sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22451	22451	0.00	28.04
22542	22542	0.00	19.96
24407	24407	0.00	20.31
20853	20853	0.00	13.50
21258	21258	0.00	14.46
21329	21329	0.00	25.83
21595	21595	0.00	18.65
21957	22451	1.30	28.43
21094	21980	3.01	23.34
21584	21980	2.87	19.81
21980	21980	0.00	24.68
22323	21980	5.41	20.66

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Potassium citrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20021-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potassium citrate; Kalii citras

Special notes

When selecting the *Potassium citrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Potassium citrate	7	10	116

Second-stage model

For differentiation of the substance/substance group *Potassium citrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium citrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Potassium citrate	11320212	20655	40	20111201
Caelo	Potassium citrate	13317618	21452	60	20130926
Caelo	Potassium citrate	15123103	21775	60	20150414
Caelo	Potassium citrate	161130	22476	60	20160602*
Euro OTC	Potassium citrate	1509044	21936	60	20151013*
Euro OTC	Potassium citrate	1611017	22921	40	20161207*
Euro OTC	Potassium citrate	1912008	25090	40	20200115*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 7 reference samples from the substance/substance group *Potassium citrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 400 spectra of 10 reference samples from the substance/substance group *Potassium citrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Potassium citrate	170929	23290	40
Caelo	Potassium citrate	180385	24046	40
Caelo	Potassium citrate	191804	24736	40
Euro OTC	Potassium citrate	1603040	22521	40
Euro OTC	Potassium citrate	1606041	22676	40
Euro OTC	Potassium citrate	1705024	23428	40
Euro OTC	Potassium citrate	1803003	24084	40
Euro OTC	Potassium citrate	1807034	24160	40
Euro OTC	Potassium citrate	1902027	24485	40
Euro OTC	Potassium citrate	1907016	24785	40

- 118 742 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 287 spectra from 139 *Apo-Ident* customers from 120 batches from the substance/substance group *Potassium citrate*.
- Among them are spectra of independent samples from 116 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Potassium citrate	KNC0196J15	4
Caelo	Potassium citrate	15435710	5
Alliance	Potassium citrate	1611017-01	1
Caelo	Potassium citrate	12135309	2
Caelo	Potassium citrate	1215309	1
Caelo	Potassium citrate	14138105	6
Caelo	Potassium citrate	14138107	1
Caelo	Potassium citrate	3456	1
Caelo	Potassium citrate	5555	1
Caelo	Potassium citrate	1112008-01	1
Caelo	Potassium citrate	11102201	1
Caelo	Potassium citrate	12135303	2
Caelo	Potassium citrate	12299201	5
Caelo	Potassium citrate	12299203	4
Caelo	Potassium citrate	71730128	1
Caelo	Potassium citrate	13080602	8
Caelo	Potassium citrate	12299202	1
Caelo	Potassium citrate	13080603	1
Caelo	Potassium citrate	411025-1-P	1
Caelo	Potassium citrate	71730367	1
Caelo	Potassium citrate	13317603	2
Caelo	Potassium citrate	28021402	1
Caelo	Potassium citrate	13135908	1

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Supplier	Substance	Batch	Spectra
Caelo	Potassium citrate	13317602	2
Caelo	Potassium citrate	123Testmessung	1
Caelo	Potassium citrate	12334	1
Caelo	Potassium citrate	123Test	4
Caelo	Potassium citrate	17061402	1
Caelo	Potassium citrate	123test	2
Caelo	Potassium citrate	5021509	1
Caelo	Potassium citrate	14138119	1
Caelo	Potassium citrate	189645	1
Caelo	Potassium citrate	15123102	2
Caelo	Potassium citrate	15148701	7
Caelo	Potassium citrate	12345678	1
Caelo	Potassium citrate	123654879	1
Caelo	Potassium citrate	12648	1
Caelo	Potassium citrate	12456	1
Caelo	Potassium citrate	15435701	6
Caelo	Potassium citrate	151231	1
Caelo	Potassium citrate	12345	1
Caelo	Potassium citrate	154357	3
Caelo	Potassium citrate	16113003	1
Caelo	Potassium citrate	232262310107	1
Caelo	Potassium citrate	16113006	4
Caelo	Potassium citrate	15435711	1
Caelo	Potassium citrate	17092904	2
Caelo	Potassium citrate	18007603	1
Caelo	Potassium citrate	170922904	1
Caelo	Potassium citrate	18038506	3
Caelo	Potassium citrate	18038502	2
Caelo	Potassium citrate	18038519	1
Caelo	Potassium citrate	16113012	5
Caelo	Potassium citrate	11320201	1
Caelo	Potassium citrate	13135907	5
Caelo	Potassium citrate	15148706	9
Caelo	Potassium citrate	9259107	1
Caelo	Potassium citrate	12135302	6
Caelo	Potassium citrate	154357025	1
Caelo	Potassium citrate	2114M1737	1
Caelo	Potassium citrate	15148707	4
Caelo	Potassium citrate	9259120	1
Caelo	Potassium citrate	1234	4
Caelo	Potassium citrate	3012Q-01737	1
Caelo	Potassium citrate	18038512	1
Caelo	Potassium citrate	16113007	2
Caelo	Potassium citrate	17092903	1
Caelo	Potassium citrate	18038507	1
Caelo	Potassium citrate	1204016-01	1
Caelo	Potassium citrate	13317604	2
Caelo	Potassium citrate	16113002	3
Caelo	Potassium citrate	15435702	1
Caelo	Potassium citrate	12135311	1
Caelo	Potassium citrate	13135904	1
Caelo	Potassium citrate	16113008	1
Caelo	Potassium citrate	14138118	2
Caelo	Potassium citrate	15148702	1
Caelo	Potassium citrate	15435703	2
Caelo	Potassium citrate	15435709	2
Caelo	Potassium citrate	15434709	1
Caelo	Potassium citrate	gfte	1
Caelo	Potassium citrate	3112M01737	1
Caelo	Potassium citrate	13135902	1

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Supplier	Substance	Batch	Spectra
Caelo	Potassium citrate	13317613	2
Caelo	Potassium citrate	15158706	1
Caelo	Potassium citrate	1543702	1
EuRho/Phönix	Potassium citrate	1311036-01	1
Euro OT/Phönix	Potassium citrate	3036325	1
Euro OTC	Potassium citrate	22101303	1
Euro OTC	Potassium citrate	123456	6
Euro OTC	Potassium citrate	1603040-01	12
Euro OTC	Potassium citrate	160601-01	1
Euro OTC	Potassium citrate	160604101	1
Euro OTC	Potassium citrate	160604-01	1
Euro OTC	Potassium citrate	1306032-01	1
Euro OTC	Potassium citrate	1902027-01	2
Euro OTC	Potassium citrate	1705024-01	6
Euro OTC	Potassium citrate	1803003-01	1
Euro OTC	Potassium citrate	16113012	1
Euro OTC	Potassium citrate	1807034-01	1
Euro OTC	Potassium citrate	1406025-01	1
Euro OTC	Potassium citrate	1611017-01	6
EuRoh/Noweda	Potassium citrate	1807034-01	1
Euro OTC	Potassium citrate	190701601	1
Euro OTC	Potassium citrate	1311036-01	9
Euro OTC	Potassium citrate	1410014-01	2
Euro OTC	Potassium citrate	1504024-01	2
Euro OTC	Potassium citrate	1509044-01	5
Euro OTC	Potassium citrate	1606041-01	4
Fagron	Potassium citrate	1234567	1
Gatt-Koller	Potassium citrate	1800758	1
ghfgh	Potassium citrate	3654645	1
Gutenberg-Apotheke	Potassium citrate	13135907	1
L12	Potassium citrate	15435709	1
Labor	Potassium citrate	1234	2
lohmann	Potassium citrate	1051470	1
Nachprüfung	Potassium citrate	111112	1
Nachprüfung	Potassium citrate	123456	1
Noweda 10.12.2019	Potassium citrate	18007607	1
Euro OTC	Potassium citrate	1915A-01737	1
Phoenix	Potassium citrate	1326PLV-1739	1
Phoenix	Potassium citrate	15148708	1
Phoenix 08.07.2014	Potassium citrate	13317624	1
Phoenix Goettin	Potassium citrate	13317613	1
Phönix	Potassium citrate	1211006-01	2
Phönix	Potassium citrate	15123103	1
Sanacorb	Potassium citrate	12135311	2
Sanacorp	Potassium citrate	160604101	1
Sanacorp/ euRho	Potassium citrate	1204016-01	1
Caelo	Potassium citrate		8
Caelo	Potassium citrate	11320212	3
Caelo	Potassium citrate	13317618	2
Caelo	Potassium citrate	15123103	4
Fagron	Potassium citrate		1
Hiperscan	Potassium citrate		1
HiperScan	Potassium citrate		1
Testsubstanz	Potassium citrate		1

- 110 960 spectra from 742 *Apo-Ident* customers from a total of 31 782 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Potassium citrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium citrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	400	0	118 742
Type C	0	287	0	110 960

The substance/substance group *Potassium citrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 97.9094 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium citrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ribavirin	41.15	—
Neomycin sulfate	44.18	—
Levothyroxin sodium	47.66	—
Sodium cromoglicate	51.12	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium citrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20655	22476	3.73	43.31
21452	22476	4.27	44.61
22921	22921	0.00	42.20
25090	25090	0.00	42.06
21775	22476	3.03	42.89
21936	21936	0.00	40.64
22476	22476	0.00	43.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Potassium hydrogen tartrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20509-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potassium hydrogen tartrate; Kalii hydrogentartras

Special notes

When selecting the *Potassium hydrogen tartrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Potassium hydrogen tartrate	4	2	22

Second-stage model

For differentiation of the substance/substance group *Potassium hydrogen tartrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium hydrogen tartrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Potassium hydrog...	11345805	20772	40	20120103
Caelo	Potassium hydrog...	15354609	23193	40	20151030
Caelo	Potassium hydrog...	170656	23285	40	20170511*
Caelo	Potassium hydrog...	182051	24763	40	20180903*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Potassium hydrogen tartrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Potassium hydrogen tartrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Potassium hydrogen tartrate	17065604	23414	40
Caelo	Potassium hydrogen tartrate	17065603	23709	40
Caelo	Potassium hydrogen tartrate	11345805	20644	40
Caelo	Potassium hydrogen tartrate	11345805	20645	40

- 118 982 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 36 spectra from 26 *Apo-Ident* customers from 23 batches from the substance/substance group *Potassium hydrogen tartrate*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bären Apotheke	Potassium hydrogen tartrate	15354613	1
Caelo	Potassium hydrogen tartrate	15354601	1
Caelo	Potassium hydrogen tartrate	11127417	1
Caelo	Potassium hydrogen tartrate	11345807	1
Caelo	Potassium hydrogen tartrate	17061303	1
Caelo	Potassium hydrogen tartrate	13030006	2
Caelo	Potassium hydrogen tartrate	23062015A	1
Caelo	Potassium hydrogen tartrate	15081010	1
Caelo	Potassium hydrogen tartrate	15354604	2
Caelo	Potassium hydrogen tartrate	1534609	1
Caelo	Potassium hydrogen tartrate	15354613	1
Caelo	Potassium hydrogen tartrate	15354614	2
Caelo	Potassium hydrogen tartrate	18205104	1
Caelo	Potassium hydrogen tartrate	13133114	1
Caelo	Potassium hydrogen tartrate	15081005	1
Caelo	Potassium hydrogen tartrate	15081008	2
Caelo	Potassium hydrogen tartrate	13133104	2
Caelo	Potassium hydrogen tartrate	160514b	1
Caelo	Potassium hydrogen tartrate	90573259	1
Caelo	Potassium hydrogen tartrate	13133120	2
Gehe	Potassium hydrogen tartrate	11345808	1
Lamotte/Phönix	Potassium hydrogen tartrate	17065602	1
Caelo	Potassium hydrogen tartrate	14115208	1
phönix	Potassium hydrogen tartrate	15354604	1
Sanacorp	Potassium hydrogen tartrate	14115208	3
Sanacorp	Potassium hydrogen tartrate	15354609	1
Caelo	Potassium hydrogen tartrate	15354609	2

- 111 211 spectra from 742 *Apo-Ident* customers from a total of 31 868 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Potassium hydrogen tartrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium hydrogen tartrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	160	0	118 982
Type C	0	35	1	111 211

The substance/substance group *Potassium hydrogen tartrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	97.2222 % (> 88.8889 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium hydrogen tartrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	57.56	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium hydrogen tartrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24763	24763	0.00	56.85
20772	24763	5.85	55.38
23193	24763	2.72	56.40
23285	23285	0.00	56.94

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Potassium sodium tartrate tetrahydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20782-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potassium sodium tartrate tetrahydrate; Kalii natrii tartras tetrahydricus

Special notes

When selecting the *Potassium sodium tartrate tetrahydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Potassium sodium tartrate tetrahydrate	3	2	2

Second-stage model

For differentiation of the substance/substance group *Potassium sodium tartrate tetrahydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium sodium tartrate tetrahydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Potassium sodium...	12030207	20782	40	20120213
Caelo	Potassium sodium...	13216605	20998	40	1404530
Caelo	Potassium sodium...	14376001	21801	60	20150204

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Potassium sodium tartrate tetrahydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Potassium sodium tartrate tetrahydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Potassium sodium tartrate te...	15375607	23207	40
Caelo	Potassium sodium tartrate te...	172577	23824	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 16 spectra from 6 *Apo-Ident* customers from 2 batches from the substance/substance group *Potassium sodium tartrate tetrahydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Potassium sodium tartrate te...	15375601	12
Caelo	Potassium sodium tartrate te...	17257701	4

- 111 231 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Potassium sodium tartrate tetrahydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium sodium tartrate tetrahydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	16	0	111 231

The substance/substance group *Potassium sodium tartrate tetrahydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium sodium tartrate tetrahydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Aciclovir	44.51	—
Levothyroxin sodium	45.23	—
Sodium cromoglicate	45.48	—
Fructose	51.16	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium sodium tartrate tetrahydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20782	20998	4.65	50.47
20998	20998	0.00	50.14
21801	20998	8.66	47.71

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Potassium sorbate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20020-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potassium sorbate; Kalii sorbas

Special notes

When selecting the *Potassium sorbate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Potassium sorbate	6	8	134

Second-stage model

For differentiation of the substance/substance group *Potassium sorbate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium sorbate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Potassium sorbate	13224604	21444	60	20130813
Caelo	Potassium sorbate	163266	23059	40	20170105*
Caelo	Potassium sorbate	17170008	23585	30	20170711
Euro OTC	Potassium sorbate	1508025	21892	60	20150902*
Euro OTC	Potassium sorbate	1608013	22786	40	20160819*
Euro OTC	Potassium sorbate	1907023	24764	40	20190802*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 270 spectra of 6 reference samples from the substance/substance group *Potassium sorbate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 419 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 8 reference samples from the substance/substance group *Potassium sorbate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Potassium sorbate	171700	23638	40
Caelo	Potassium sorbate	173451	23830	40
Caelo	Potassium sorbate	181650	24224	40
Caelo	Potassium sorbate	191072	24539	40
Euro OTC	Potassium sorbate	1703034	23176	40
Euro OTC	Potassium sorbate	1710015	23772	40
Euro OTC	Potassium sorbate	1805029	24126	40
Euro OTC	Potassium sorbate	1901020	24464	40

- 118 822 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 834 spectra from 458 *Apo-Ident* customers from 139 batches from the substance/substance group *Potassium sorbate*.
- Among them are spectra of independent samples from 134 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Potassium sorbate	13065216	1
AHD	Potassium sorbate	17345116	1
Euro OTC	Potassium sorbate	15382115	1
Caelo	Potassium sorbate	13065205	12
Alliance Healthcare	Potassium sorbate	15382115	1
Allianz	Potassium sorbate	17170006	1
Anzag	Potassium sorbate	12211107	1
Anzag	Potassium sorbate	15382114	2
Anzag 12.01.15	Potassium sorbate	13224611	1
Caelo	Potassium sorbate	11261304	3
Apomix/Noweda	Potassium sorbate	13224611	1
Bombastus	Potassium sorbate	14380632	1
Caelo	Potassium sorbate	18165015	5
Caelo	Potassium sorbate	11214207	1
Caelo	Potassium sorbate	12345	1
Caelo	Potassium sorbate	1205999	1
Caelo	Potassium sorbate	3512M-01748	1
Caelo	Potassium sorbate	20021112-2	1
Caelo	Potassium sorbate	12211107	15
Caelo	Potassium sorbate	12059914	2
Caelo	Potassium sorbate	91623299	2
Caelo	Potassium sorbate	12211102	4
Caelo	Potassium sorbate	13065204	11
Caelo	Potassium sorbate	12211108	2
Caelo	Potassium sorbate	12211121	4
Caelo	Potassium sorbate	K-010213-1	1
Caelo	Potassium sorbate	13065216	11
Caelo	Potassium sorbate	13065217	11
Caelo	Potassium sorbate	12059902	1
Caelo	Potassium sorbate	200613K1	1

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Supplier	Substance	Batch	Spectra
Caelo	Potassium sorbate	13065211	1
Caelo	Potassium sorbate	2041402	1
Caelo	Potassium sorbate	11192305	3
Caelo	Potassium sorbate	13065222	1
Caelo	Potassium sorbate	13224608	2
Caelo	Potassium sorbate	13111409	1
Caelo	Potassium sorbate	13224610	1
Caelo	Potassium sorbate	14380607	5
Caelo	Potassium sorbate	14380606	9
Caelo	Potassium sorbate	1438060	2
Caelo	Potassium sorbate	14380612	2
Caelo	Potassium sorbate	15248203	3
Caelo	Potassium sorbate	14380613	1
Caelo	Potassium sorbate	14380633	16
Caelo	Potassium sorbate	111033102	1
Caelo	Potassium sorbate	143806	1
Caelo	Potassium sorbate	14380635	7
Caelo	Potassium sorbate	16156505	1
Caelo	Potassium sorbate	16326607	16
Caelo	Potassium sorbate	14380618	1
Caelo	Potassium sorbate	16326602	2
Caelo	Potassium sorbate	16326608	18
Caelo	Potassium sorbate	14380631	1
Caelo	Potassium sorbate	27101705	1
Caelo	Potassium sorbate	17170005	1
Caelo	Potassium sorbate	17170006	7
Caelo	Potassium sorbate	16326615	1
Caelo	Potassium sorbate	1/1/0017	1
Caelo	Potassium sorbate	90318101	1
Caelo	Potassium sorbate	17345105	1
Caelo	Potassium sorbate	9061806	1
Caelo	Potassium sorbate	17345104	33
Caelo	Potassium sorbate	7111805	1
Caelo	Potassium sorbate	18165006	11
Caelo	Potassium sorbate	17170018	1
Caelo	Potassium sorbate	14380601	18
Caelo	Potassium sorbate	17170007-20171106Ma1	1
Caelo	Potassium sorbate	17170012	2
Caelo	Potassium sorbate	15248205	11
Caelo	Potassium sorbate	1816510	1
Caelo	Potassium sorbate	12059905	2
Caelo	Potassium sorbate	16326609	15
Caelo	Potassium sorbate	1608013-01	1
Caelo	Potassium sorbate	3354	1
Caelo	Potassium sorbate	1312024-01	2
Caelo	Potassium sorbate	17170017	10
Caelo	Potassium sorbate	12059908	2
Caelo	Potassium sorbate	14380621	10
Caelo	Potassium sorbate	14380632	18
Caelo	Potassium sorbate	16326606	13
Caelo	Potassium sorbate	17170014	19
Caelo	Potassium sorbate	13224611	11
Caelo	Potassium sorbate	15382103	1
Caelo	Potassium sorbate	15382115	8
Caelo	Potassium sorbate	13277804	1
Caelo	Potassium sorbate	12211123	1
Caelo	Potassium sorbate	15382114	9
Caelo	Potassium sorbate	912331023	1
Caelo	Potassium sorbate	12211101	10
Caelo	Potassium sorbate	14380627	8

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Supplier	Substance	Batch	Spectra
Caelo	Potassium sorbate	18165010	20
Caelo	Potassium sorbate	14140007	1
Caelo	Potassium sorbate	10199505	1
Caelo	Potassium sorbate	10012210	1
Caelo	Potassium sorbate	14192605	2
Caelo	Potassium sorbate	15382105	15
Caelo	Potassium sorbate	14380620	6
Caelo	Potassium sorbate	15382106	1
Caelo	Potassium sorbate	17170013	22
Caelo	Potassium sorbate	18165014	7
Caelo	Potassium sorbate	19107203	1
Caelo	Potassium sorbate	14380602	2
Caelo	Potassium sorbate	17345103	24
Caelo	Potassium sorbate	9305601	2
Caelo	Potassium sorbate	13224612	18
Caelo	Potassium sorbate	14380610	12
Caelo	Potassium sorbate	15248204	19
Caelo	Potassium sorbate	17170007	18
Caelo	Potassium sorbate	1112331024	1
Caelo	Potassium sorbate	14380622	9
Caelo	Potassium sorbate	17345116	20
Caelo	Potassium sorbate	17345113	1
Caelo	Potassium sorbate	317331021	1
Caelo	Potassium sorbate	12059909	4
Caesar & Loretz GmbH	Potassium sorbate	11261303	1
Caesar & Loretz GmbH	Potassium sorbate	14380627	1
Caesar & Loretz GmbH	Potassium sorbate	17170006	1
Caesar & Loretz GmbH	Potassium sorbate	17345103	1
Caesar & Loretz GmbH	Potassium sorbate	18165010	3
Caesar & Loretz GmbH	Potassium sorbate	18165004	1
Caesar & Loretz GmbH	Potassium sorbate	18165014	2
Caesar & Loretz GmbH / ...	Potassium sorbate	15382114	1
Caesar & Loretz GmbH / ...	Potassium sorbate	17345103	1
Caesar & Loretz GmbH Hi...	Potassium sorbate	13065217	2
Caesar & Loretz/Noweda	Potassium sorbate	14380621	1
Caesar & Loretz/Sanacorp	Potassium sorbate	17345104	1
Caesar&Loretz GmbH	Potassium sorbate	14380622	1
Caesar&Loretz GmbH	Potassium sorbate	17170014	1
Caesar&Loretz GmbH/Sana...	Potassium sorbate	14380607	1
Caesar/Lorenz	Potassium sorbate	13065204	1
canea, gehe	Potassium sorbate	13065215	1
cealo	Potassium sorbate	16326607	1
Cealo	Potassium sorbate	1710013	1
Cealo/ Noweda	Potassium sorbate	17345103	1
Euro OTC	Potassium sorbate	1508025-01	7
Euro OTC	Potassium sorbate	1312024-01	3
Euro OTC	Potassium sorbate	14380622	1
Euro OTC	Potassium sorbate	1608013-01	4
Euro OTC	Potassium sorbate	17170013	1
Euro OTC	Potassium sorbate	1111038-02	2
Euro OTC	Potassium sorbate	1111038-01	1
Euro OTC	Potassium sorbate	216331021	1
Euro OTC	Potassium sorbate	1710012-01	1
Euro OTC	Potassium sorbate	111103802	1
Euro OTC	Potassium sorbate	180529-01	1
Euro OTC	Potassium sorbate	13224612	1
Fagron	Potassium sorbate	1114331022	1
Fagron	Potassium sorbate	3912A-01748	1
Fagron	Potassium sorbate	4314U-01748	1
Fagron	Potassium sorbate	3115M-01748	1

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Supplier	Substance	Batch	Spectra
Fagron	Potassium sorbate	17170013	2
Fagron	Potassium sorbate	13065217	1
Fresenius	Potassium sorbate	220214221	1
gehe	Potassium sorbate	17170014	1
Gehe	Potassium sorbate	11261304	1
Gehe	Potassium sorbate	13065205	1
Gehe	Potassium sorbate	13065216	1
Gehe	Potassium sorbate	14380632	1
Gehe	Potassium sorbate	16326606	1
Gehe	Potassium sorbate	17170007	1
Gehe	Potassium sorbate	17170013	1
Gehe	Potassium sorbate	17345116	1
Gehe	Potassium sorbate	18165014	1
GEHE	Potassium sorbate	17170008	1
Gehe / Spinnrad	Potassium sorbate	216331021	1
Ichthyol/Noweda	Potassium sorbate	13224604	1
Jenne	Potassium sorbate	17170007	1
Kehr	Potassium sorbate	16326607	1
Kehr	Potassium sorbate	18165006	1
Kehr/Spinnrad	Potassium sorbate	317331021	1
Noweda	Potassium sorbate	12211101	1
Noweda	Potassium sorbate	13065222	1
Noweda	Potassium sorbate	15382115	1
Noweda	Potassium sorbate	16326606	1
Noweda	Potassium sorbate	17345103	1
Noweda / Spinnrad	Potassium sorbate	216331021	1
Caelo	Potassium sorbate	17170002	4
p&m cosmetics/gehe	Potassium sorbate	17170014	1
Phoenix	Potassium sorbate	1397235	1
Phoenix	Potassium sorbate	14380627	1
Phoenix	Potassium sorbate	216331021	1
Phoenix	Potassium sorbate	17170012	1
Phoenix	Potassium sorbate	17170017	1
Phoenix	Potassium sorbate	17345104	1
phönix	Potassium sorbate	14380632	1
phönix	Potassium sorbate	16326608	1
Phönix	Potassium sorbate	16326607	1
Phönix	Potassium sorbate	17345116	1
Fagron	Potassium sorbate	14380622	1
Phönix/Spinnrad	Potassium sorbate	1117331022	1
sana	Potassium sorbate	13224612	1
Sanacorp	Potassium sorbate	12211101	1
Sanacorp	Potassium sorbate	13065217	1
Sanacorp	Potassium sorbate	13224611	1
Sanacorp	Potassium sorbate	14380610	1
Sanacorp	Potassium sorbate	17170007	1
Bombastus	Potassium sorbate	1117331022	1
Caelo	Potassium sorbate	AKD10	1
siehe WE-Prüfprotokoll	Potassium sorbate	61/11	1
Sonnenberg-Apotheke	Potassium sorbate	13224604	1
spinnrad	Potassium sorbate	1114331022	1
spinnrad	Potassium sorbate	216331021	1
spinnrad	Potassium sorbate	2233102	1
spinnrad	Potassium sorbate	1118331022	1
Spinnrad	Potassium sorbate	111033102	1
Spinnrad	Potassium sorbate	312331021	2
Spinnrad	Potassium sorbate	912331023	4
Spinnrad	Potassium sorbate	1114331022	3
Spinnrad	Potassium sorbate	214331021	1
Spinnrad	Potassium sorbate	315331021	2

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Supplier	Substance	Batch	Spectra
Spinnrad	Potassium sorbate	815331022	2
Spinnrad	Potassium sorbate	216331021	2
Spinnrad	Potassium sorbate	616331022	2
Spinnrad	Potassium sorbate	317331021	3
Spinnrad	Potassium sorbate	1117331022	2
Spinnrad - Noweda	Potassium sorbate	315331021	1
Spinnrad / Gehe	Potassium sorbate	616331022	1
Spinnrad / Gehe	Potassium sorbate	317331021	2
spinnrad GmbH	Potassium sorbate	616331022	1
Spinnrad GmbH	Potassium sorbate	111033102	1
Spinnrad GmbH	Potassium sorbate	912331023	2
Spinnrad GmbH	Potassium sorbate	1114331022	1
Spinnrad GmbH	Potassium sorbate	214331021	1
Spinnrad GmbH / Noweda ...	Potassium sorbate	1117331022	1
Spinnrad/ Gehe 18.01.19	Potassium sorbate	317331021	1
spinnrad/gehe	Potassium sorbate	216331021	1
Spinnrad/Gehe	Potassium sorbate	315331021	1
Spinnrad/Noweda	Potassium sorbate	1117331022	1
Spinnrad/Noweda	Potassium sorbate	1118331022	1
Spinnrad/Sannacorp	Potassium sorbate	616331022	1
Spinrad/Phönix	Potassium sorbate	218331021	1
WE: über Eyach 5g/2,87E...	Potassium sorbate	14380601	1
	Potassium sorbate	10012203	1
	Potassium sorbate	12211101	2
Caelo	Potassium sorbate	17170008	17
Caelo	Potassium sorbate	13224604	16
	Potassium sorbate	17170017	1
Caelo	Potassium sorbate		1
s.Prüfprotokoll	Potassium sorbate		1
	Potassium sorbate		1

- 110 413 spectra from 742 *Apo-Ident* customers from a total of 31 757 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Potassium sorbate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium sorbate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	270	0	110 419
Type B	0	320	0	118 822
Type C	0	768	66	110 413

The substance/substance group *Potassium sorbate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.7778 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 99.8899 %)	92.0863 % (> 91.7266 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium sorbate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Finasteride (form III)	54.00	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium sorbate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24764	24764	0.00	52.22
23059	23059	0.00	58.49
23585	23059	7.74	55.98
21444	21892	9.54	52.40
21892	21892	0.00	52.05
22786	22786	0.00	52.72

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Potassium tartrate hemihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20999-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Potassium tartrate hemihydrate; Kalii tartras hemihydricus

Special notes

When selecting the *Potassium tartrate hemihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Potassium tartrate hemihydrate	5	2	13

Second-stage model

For differentiation of the substance/substance group *Potassium tartrate hemihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Potassium tartrate hemihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Potassium tartra...	13331104	21440	60	20131002
Caelo	Potassium tartra...	15167701	21812	60	20150608
Caelo	Potassium tartra...	160289	22462	60	20160405*
Caelo	Potassium tartra...	192911	25067	40	20191125*
Caelo	Potassium tartra...	193079	25096	40	20191125*

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *Potassium tartrate hemihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Potassium tartrate hemihydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Potassium tartrate hemihydrate	13331101	20999	40
Caelo	Potassium tartrate hemihydrate	182203	24248	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 14 spectra from 5 *Apo-Ident* customers from 13 batches from the substance/substance group *Potassium tartrate hemihydrate*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Potassium tartrate hemihydrate	11225007	1
Caelo	Potassium tartrate hemihydrate	27061304	1
Caelo	Potassium tartrate hemihydrate	12322110	1
Caelo	Potassium tartrate hemihydrate	13111415	1
Caelo	Potassium tartrate hemihydrate	13331113	1
Caelo	Potassium tartrate hemihydrate	15167703	1
Caelo	Potassium tartrate hemihydrate	24061705	1
Caelo	Potassium tartrate hemihydrate	17176002	2
Caelo	Potassium tartrate hemihydrate	19051804	1
Caelo	Potassium tartrate hemihydrate	17176004	1
Caelo	Potassium tartrate hemihydrate	18220301	1
Caelo	Potassium tartrate hemihydrate	17176007	1
Caelo	Potassium tartrate hemihydrate	17176001	1

- 111 233 spectra from 742 *Apo-Ident* customers from a total of 31 878 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Potassium tartrate hemihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Potassium tartrate hemihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	80	0	119 062
Type C	0	14	0	111 233

The substance/substance group *Potassium tartrate hemihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Potassium tartrate hemihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glucose monohydrate	35.28	—
Lactose monohydrate	40.67	—
Aciclovir	55.82	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Potassium tartrate hemihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21440	22462	2.19	48.14
25067	25067	0.00	44.48
25096	25096	0.00	46.90
21812	22462	2.25	47.91
22462	22462	0.00	50.82

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Povidone 25, soluble**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20684-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Povidone 25, soluble; Povidonum 25, solubile

Special notes

When selecting the *Povidone 25, soluble* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Povidone 25, soluble	9	6	33

Second-stage model

For differentiation of the substance/substance group *Povidone 25, soluble* the following second-stage model is used:

- [Submodel 5](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Povidone 25, soluble*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Povidone 25, sol. ...	12032714	20684	40	1402437
Caelo	Povidone 25, sol. ...	14142103	21378	40	AR-15-FG-000596-01
Caelo	Povidone 25, sol. ...	16307808	23255	40	AR-17-FG-015299-02
Caelo	Povidone 25, sol. ...	180276	24044	40	20180202*
Caelo	Povidone 25, sol. ...	191752	24746	40	20190717*
Caelo	Povidone 25, sol. ...	191276	24754	40	20190517*
Fagron	Povidone 25, sol. ...	12E22-N05	20770	40	1411537
Fagron	Povidone 25, sol. ...	13J21-N02	22731	40	AR-16-FG-019116-01
Fagron	Povidone 25, sol. ...	15C12-B02-323006	23265	40	1710348

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 9 reference samples from the substance/substance group *Povidone 25, soluble*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 329 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 240 spectra of 6 reference samples from the substance/substance group *Povidone 25, soluble*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Povidone 25, soluble	172091	23619	40
Caelo	Povidone 25, soluble	180766	24245	40
Caelo	Povidone 25, soluble	181820	24246	40
Caelo	Povidone 25, soluble	182383	24291	40
Caelo	Povidone 25, soluble	183000	24396	40
Caelo	Povidone 25, soluble	192500	24899	40

- 118 902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 60 spectra from 29 *Apo-Ident* customers from 36 batches from the substance/substance group *Povidone 25, soluble*.
- Among them are spectra of independent samples from 33 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alliance	Povidone 25, soluble	16307808	1
Alliance	Povidone 25, soluble	17209106	1
Alliance	Povidone 25, soluble	18112201	1
Audor Pharma	Povidone 25, soluble	18112201	1
Caelo	Povidone 25, soluble	17209104	3
Caelo	Povidone 25, soluble	12376301	1
Caelo	Povidone 25, soluble	13323407	2
Caelo	Povidone 25, soluble	14142109	3
Caelo	Povidone 25, soluble	14207508	3
Caelo	Povidone 25, soluble	14207511	4
Caelo	Povidone 25, soluble	14207517	1
Caelo	Povidone 25, soluble	15383103	2
Caelo	Povidone 25, soluble	16051102	1
Caelo	Povidone 25, soluble	15383101	3
Caelo	Povidone 25, soluble	16051104	1
Caelo	Povidone 25, soluble	16051108	1
Caelo	Povidone 25, soluble	163078085328	1
Caelo	Povidone 25, soluble	16307809	3
Caelo	Povidone 25, soluble	18027602	2
Caelo	Povidone 25, soluble	18238302	1
Caelo	Povidone 25, soluble	18300003	1
Caelo	Povidone 25, soluble	17209103	1
Caelo	Povidone 25, soluble	18182002	2
Caelo	Povidone 25, soluble	18024602	1
Caelo	Povidone 25, soluble	16051110	1

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Supplier	Substance	Batch	Spectra
Caelo	Povidone 25, soluble	18112201	2
Caelo	Povidone 25, soluble	16307811	1
Caelo	Povidone 25, soluble	16051101	2
Caelo	Povidone 25, soluble	14207515	1
Caelo	Povidone 25, soluble	16307812	1
Caelo	Povidone 25, soluble	15383102	1
Caesar & Loretz GmbH	Povidone 25, soluble	18300002	1
Fagron	Povidone 25, soluble	11276509T0	1
Fagron	Povidone 25, soluble	24701988Q0	1
Fagron	Povidone 25, soluble	15C12-B02-327866	1
Gehe	Povidone 25, soluble	18300002	1
GEHE	Povidone 25, soluble	18112201	1
Caelo	Povidone 25, soluble	18300006	1
Caelo	Povidone 25, soluble	12032714	1
Caelo	Povidone 25, soluble	14142103	1
Caelo	Povidone 25, soluble	16307808	1

- 111 187 spectra from 742 *Apo-Ident* customers from a total of 31 856 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Povidone 25, soluble* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Povidone 25, soluble* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	240	0	118 902
Type C	0	60	0	111 187

The substance/substance group *Povidone 25, soluble* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 90.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Povidone 25, soluble* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Povidone iodine	7.29	16.26
Norethisterone acetate	19.84	—
Hydrocortisone	21.41	—
Fusidic acid	21.91	47.27
Budesonide, micronized	28.24	—
Progesterone, micronized	29.13	—
Estradiol valerate	30.13	—
Methylcellulose	35.30	—
Pregnenolone	41.39	—
Testosterone	41.58	—
Testosterone propionate	49.36	—
Menthol	53.66	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Povidone 25, soluble* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22731	22731	0.00	35.42
24044	24044	0.00	17.86
20684	20684	0.00	15.21
20770	20770	0.00	19.62
23265	23265	0.00	21.05
23255	23255	0.00	14.30
21378	21378	0.00	13.62
24754	24754	0.00	28.26
24746	24746	0.00	26.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Povidone iodine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20472-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Povidone iodine; Povidonum iodinatum

Special notes

When selecting the *Povidone iodine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Povidone iodine	10	5	30

Second-stage model

For differentiation of the substance/substance group *Povidone iodine* the following second-stage model is used:

- [Submodel 5](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Povidone iodine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Povidone iodine	13337205	21466	60	20131021
Caelo	Povidone iodine	15234101	23252	40	AR-17-FG-015433-02
Caelo	Povidone iodine	15234109	23256	40	20150717
Caelo	Povidone iodine	182385	24234	40	20180917*
Euro OTC	Povidone iodine	1501029-01	21777	60	20150211
Euro OTC	Povidone iodine	1509009	21908	60	20150918*
Euro OTC	Povidone iodine	1606026-02	23906	40	20160708
Euro OTC	Povidone iodine	1805007	24118	40	20180525*
Euro OTC	Povidone iodine	1905008	24770	40	20190628*
Euro OTC	Povidone iodine	2001048	25122	40	20200320*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 10 reference samples from the substance/substance group *Povidone iodine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 229 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 200 spectra of 5 reference samples from the substance/substance group *Povidone iodine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Povidone iodine	180763	24261	40
Caelo	Povidone iodine	192297	24879	40
Euro OTC	Povidone iodine	1110013-02	21073	40
Euro OTC	Povidone iodine	1606026	22675	40
Euro OTC	Povidone iodine	1704007	23435	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 70 spectra from 31 *Apo-Ident* customers from 34 batches from the substance/substance group *Povidone iodine*.
- Among them are spectra of independent samples from 30 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
BASF, Noweda	Povidone iodine	1110013-02	1
Basf/Sanacorp	Povidone iodine	180500701	1
Caelo	Povidone iodine	12072605	1
Caelo	Povidone iodine	11168607	1
Caelo	Povidone iodine	12153106	2
Caelo	Povidone iodine	1110013-02	1
Caelo	Povidone iodine	11168612	1
Caelo	Povidone iodine	12153110	2
Caelo	Povidone iodine	12153116	2
Caelo	Povidone iodine	19061302	1
Caelo	Povidone iodine	15121402	1
Caelo	Povidone iodine	14195810	2
Caelo	Povidone iodine	1407032-01	1
Caelo	Povidone iodine	15442405	1
Caelo	Povidone iodine	17028102	2
Euro OTC	Povidone iodine	1401029-01	1
Euro OTC	Povidone iodine	1509009-02	2
Euro OTC	Povidone iodine	1606026	1
Euro OTC	Povidone iodine	8051808	1
Euro OTC	Povidone iodine	1704007-01	1
Euro OTC	Povidone iodine	1805007-02	2
Euro OTC	Povidone iodine	110013-02	1
Euro OTC	Povidone iodine	1603023-01	2
Euro OTC	Povidone iodine	1110013-02	4
Euro OTC	Povidone iodine	130901001	1
Euro OTC	Povidone iodine	111001302	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Povidone iodine	1509009-01	1
Euro OTC	Povidone iodine	1407032-01	5
Euro OTC	Povidone iodine	G4208BPZ0	2
Euro OTC	Povidone iodine	1805007-01	5
Euro/ Jenne	Povidone iodine	1606026-02	4
Euroo/Phoenix	Povidone iodine	G3115BPZ0	1
Euroo/Sana	Povidone iodine	1501029-01	3
Fagron	Povidone iodine	1110013-02	1
Noweda	Povidone iodine	G0354BPZ0	1
Phönix	Povidone iodine	1110013-02	1
Stumpf	Povidone iodine	11168612	1
Caelo	Povidone iodine	12153119	2
Caelo	Povidone iodine	15234101	1
Caelo	Povidone iodine	15234109	1
Euro OTC	Povidone iodine	1606026-02	4

- 111 177 spectra from 742 *Apo-Ident* customers from a total of 31 858 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Povidone iodine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Povidone iodine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	460	0	110 229
Type B	0	200	0	118 942
Type C	0	67	3	111 177

The substance/substance group *Povidone iodine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	95.7143 % (> 91.4286 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Povidone iodine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fusidic acid	18.91	54.80
Norethisterone acetate	19.95	—
Povidone 25, soluble	22.19	18.32
Budesonide, micronized	25.41	—
Hydrocortisone	25.57	—
Estradiol valerate	25.90	—
Progesterone, micronized	34.95	—
Testosterone	42.01	—
Testosterone propionate	44.71	—
Methylcellulose	45.20	—
Menthol	52.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Povidone iodine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24770	24770	0.00	21.23
23252	23252	0.00	18.91
23256	23252	8.15	20.67
24234	24234	0.00	20.71
21908	21908	0.00	20.37
24118	24118	0.00	25.90
21777	21908	4.12	19.49
23906	21908	7.51	21.38
25122	25122	0.00	21.18
21466	21908	4.82	20.43

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prasterone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20703-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prasterone; Prasteronum

Special notes

When selecting the *Prasterone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prasterone	17	7	73

Second-stage model

For differentiation of the substance/substance group *Prasterone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prasterone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Prasterone	APZDHA16003-M	23931	40	1805404
Audor Pharma	Prasterone	APZDHAC17003MD	24412	40	20180119
Audor Pharma	Prasterone	APZDHAC18004D	24430	40	1906523
Euro OTC	Prasterone	1102036-01	20703	40	1404310
Euro OTC	Prasterone	1506011	21824	60	20150629*
Euro OTC	Prasterone	1602018	22506	30	20160301*
Euro OTC	Prasterone	1704012	23389	40	20170529*
Euro OTC	Prasterone	1707014	23695	40	20170829*
Euro OTC	Prasterone	1710035	23868	40	20171212*
Euro OTC	Prasterone	1712014	23893	40	20180115*
Euro OTC	Prasterone	1907045	24853	40	20190905*
Euro OTC	Prasterone	1809009	24966	40	20191111*
Euro OTC	Prasterone	1910025	24967	40	20191111*
Euro OTC	Prasterone	2001038	25091	40	20200302*
Fagron	Prasterone	13J10-B02-287175	20960	40	1404309
Fagron	Prasterone	15G14-B07-310827	21917	60	20150814
Fagron	Prasterone	16L13-B01-330724	23865	40	20161228

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 710 spectra of 17 reference samples from the substance/substance group *Prasterone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 17 different batches.
- 109 979 spectra from a total of 1949 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 520 spectra of 12 reference samples from the substance/substance group *Prasterone*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Audor Pharma	Prasterone	APZDHA16003-1MD	23932	40
Euro OTC	Prasterone	1702025	23147	40
Euro OTC	Prasterone	1805018	24137	40
Euro OTC	Prasterone	1809010	24318	40
Euro OTC	Prasterone	1901030	24453	40
Euro OTC	Prasterone	1901031	24454	40
Fagron	Prasterone	18C12-B01-347633	23990	40
Euro OTC	Prasterone	1506011	21824SI [†]	60
Euro OTC	Prasterone	1602018	22506SI [†]	40
Euro OTC	Prasterone	1702025	23147SI	40
Euro OTC	Prasterone	1809009	24323	40
Fagron	Prasterone	15G14-B07-310827	21917SI [†]	60

- 118 622 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 117 spectra from 33 *Apo-Ident* customers from 75 batches from the substance/substance group *Prasterone*.
- Among them are spectra of independent samples from 73 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Prasterone	AP11040002P	2
Audor Pharma	Prasterone	10050051/1P	1
Audor Pharma	Prasterone	APZDHAC17003-MD	2
Caelo	Prasterone	15A15-B40-307323	1
Caelo	Prasterone	16B19-B04-318665	1
Caelo	Prasterone	16I02-B02-326485	1
Caelo	Prasterone	16I02-B02-326485	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Prasterone	1412028-01	1
EuRho	Prasterone	1311002-01	1
Euro OTC	Prasterone	1203010-01	1
Euro OTC	Prasterone	2081302	1
Euro OTC	Prasterone	9215-4/09	1
Euro OTC	Prasterone	XPC0263	1
Euro OTC	Prasterone	1401040-01	1
Euro OTC	Prasterone	26031506	1
Euro OTC	Prasterone	30041509	1
Euro OTC	Prasterone	4091511	1
Euro OTC	Prasterone	1602018-01	3
Euro OTC	Prasterone	DHEA150801-1	1
Euro OTC	Prasterone	1702025-01	7
Euro OTC	Prasterone	1412028	1
Euro OTC	Prasterone	ZDHAC18002	1
Euro OTC	Prasterone	1809010-01	1
Euro OTC	Prasterone	23021711	1
Euro OTC	Prasterone	1805018-01	2
Euro OTC	Prasterone	1306021-01	3
Euro OTC	Prasterone	T03-04/1412028-01	1
Euro OTC	Prasterone	1702025	3
Euro OTC	Prasterone	1704012-01	1
Euro OTC	Prasterone	180901001	1
Euro OTC	Prasterone	1602018-02	2
Euro OTC	Prasterone	5101849	1
Euro OTC	Prasterone	1412028-01	4
Euro OTC	Prasterone	1506011-01	3
Euro OTC	Prasterone	18050118-01	1
Euro OTC	Prasterone	1901030-01	1
Euro OTC	Prasterone	170202501	1
Euro OTC	Prasterone	1311002-01	2
Fagron	Prasterone	12G04-N19	2
Fagron	Prasterone	12C26-N09	1
Fagron	Prasterone	19061304	1
Fagron	Prasterone	13J10-B02-287177	1
Fagron	Prasterone	14C18-B02	1
Fagron	Prasterone	14C18-B02-293606	1
Fagron	Prasterone	14C18-B02-293602	1
Fagron	Prasterone	14H12-B05-297727	2
Fagron	Prasterone	14c18b02293602	1
Fagron	Prasterone	14h12b05-297723	1
Fagron	Prasterone	DHEAA150401-1	1
Fagron	Prasterone	C04-140804(M)	1
Fagron	Prasterone	1421-B03-300211	1
Fagron	Prasterone	16B19-B04-322246	2
Fagron	Prasterone	15I18-B09-316798	1
Fagron	Prasterone	16J26-B03-327602	1
Fagron	Prasterone	27071705	1
Fagron	Prasterone	16I02-B02-326485	2
Fagron	Prasterone	16L13-B01-332104	1
Fagron	Prasterone	17D11-B10-336395	1
Fagron	Prasterone	12K30-N06	3
Fagron	Prasterone	DHEA160802	1
Fagron	Prasterone	7013260004	1
Fagron	Prasterone	18C12	1
Fagron	Prasterone	16B19-B04-318665	2
Fagron	Prasterone	18B02-B02-345147	1
Fagron	Prasterone	13J10-B02	1
Fagron	Prasterone	19G10-B02-365154	1
Fagron	Prasterone	15A15-B40-307323	1

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Supplier	Substance	Batch	Spectra
Fagron	Prasterone	18B13-B09_346424	1
Fargon	Prasterone	16B19-B04-318665	1
Fragon	Prasterone	12G04-N19	1
Gall Pharma	Prasterone	16/02-B02	1
Haihang	Prasterone	20130507	1
Haihang Industry	Prasterone	20130816	4
Kögl	Prasterone	1803108	1
Nachprüfung	Prasterone	120022	1
Fagron	Prasterone	14C18-Bo2-293603	1
NWM Shandong Northwest ...	Prasterone	PST151207	1
Euro OTC	Prasterone	1409004-01	4
Euro OTC	Prasterone	22021306	1
Audor Pharma	Prasterone	APZDHA16003-M	1
Fagron	Prasterone	15G14-B07-310827	1

- 111 130 spectra from 742 *Apo-Ident* customers from a total of 31 817 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prasterone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prasterone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	710	0	109 979
Type B	0	510	10	118 622
Type C	0	116	1	111 130

The substance/substance group *Prasterone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.1549 %)
Type B	100.0000 % (> 99.9893 %)	98.0769 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	99.1453 % (> 96.5812 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prasterone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Testosterone	20.17	—
Cholesterol	27.74	—
Norethisterone acetate	41.11	—
Deoxycholic acid	44.13	—
Methylcellulose	47.14	—
Estradiol valerate	49.55	—
Hypromellose 4000	51.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prasterone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24430	24430	0.00	30.55
23695	23695	0.00	33.72
20703	20703	0.00	43.08
20960	20960	0.00	43.88
24966	24966	0.00	48.31
23893	23893	0.00	33.68
24412	23893	1.92	32.79
21824	21824	0.00	44.09
24967	24967	0.00	41.97
22506	22506	0.00	47.75
21917	21824	8.78	41.11
23865	23695	10.54	38.40
23931	23931	0.00	32.07
25091	25091	0.00	42.25
23868	23868	0.00	25.02
23389	23389	0.00	23.59
24853	24853	0.00	36.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prednicarbate, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20196-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prednicarbate, micronized; Prednicarbatum micronisatum

Special notes

When selecting the *Prednicarbate, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednicarbate, micronized	8	13	251

Second-stage model

For differentiation of the substance/substance group *Prednicarbate, micronized* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednicarbate, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prednicarbate, m...	13119402	20832	60	1501576
Caelo	Prednicarbate, m...	13119402	20833	60	20130517
Caelo	Prednicarbate, m...	13119402	20833SI	30	20130517
Caelo	Prednicarbate, m...	13372404	21368	50	AR-15-FG-007941-02
Caelo	Prednicarbate, m...	13372404	21369	49	20131119
Caelo	Prednicarbate, m...	13372404	21369SI	33	20131119
Euro OTC	Prednicarbate, m...	1302033-02	21610	60	1509286
Euro OTC	Prednicarbate, m...	1507011	21858	60	20150730*
Euro OTC	Prednicarbate, m...	1601058	22366	45	20160223*
Euro OTC	Prednicarbate, m...	1601058	22366SI	31	20160223*
Euro OTC	Prednicarbate, m...	2001031	25119	40	20200331*
Fagron	Prednicarbate, m...	12D27-N04	20700	40	20120509
Fagron	Prednicarbate, m...	12D27-N04	20700SI	48	20120509
Fagron	Prednicarbate, m...	14A27-B02-291256	21572	60	AR-16-FG-011442-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 666 spectra of 14 reference samples from the substance/substance group *Prednicarbate, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 023 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 915 spectra of 29 reference samples from the substance/substance group *Prednicarbate, micronized*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prednicarbate, micronized	160874	22447	60
Caelo	Prednicarbate, micronized	170138	23040	40
Caelo	Prednicarbate, micronized	173156	23845	40
Caelo	Prednicarbate, micronized	172204	23848	40
Caelo	Prednicarbate, micronized	192604	24901	40
Euro OTC	Prednicarbate, micronized	1605001	22558	30
Euro OTC	Prednicarbate, micronized	1607012	22703	40
Euro OTC	Prednicarbate, micronized	1609022	22860	40
Euro OTC	Prednicarbate, micronized	1707022	23540	40
Euro OTC	Prednicarbate, micronized	1801013	23887	40
Euro OTC	Prednicarbate, micronized	1805005	24134	40
Euro OTC	Prednicarbate, micronized	1809015	24320	40
Euro OTC	Prednicarbate, micronized	1903023	24633	40
Caelo	Prednicarbate, micronized	160874	22447SI	30
Caelo	Prednicarbate, micronized	170138	23040SI	20
Caelo	Prednicarbate, micronized	173156	23845SI	20
Caelo	Prednicarbate, micronized	172204	23848SI	20
Caelo	Prednicarbate, micronized	192604	24901SI	26
Euro OTC	Prednicarbate, micronized	1507011	21858SI [†]	15
Euro OTC	Prednicarbate, micronized	1605001	22558SI	25
Euro OTC	Prednicarbate, micronized	1607012	22703SI	28
Euro OTC	Prednicarbate, micronized	1609022	22860SI	27
Euro OTC	Prednicarbate, micronized	1707022	23540SI	19
Euro OTC	Prednicarbate, micronized	1801013	23887SI	20
Euro OTC	Prednicarbate, micronized	1805005	24134SI	20
Euro OTC	Prednicarbate, micronized	1809015	24320SI	20
Euro OTC	Prednicarbate, micronized	1903023	24633SI	32
Euro OTC	Prednicarbate, micronized	2001031	25119SI [†]	27
Fagron	Prednicarbate, micronized	14A27-B02-291256	21572SI [†]	36

- 118227 spectra from a total of 2404 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1257 spectra from 417 *Apo-Ident* customers from 265 batches from the substance/substance group *Prednicarbate, micronized*.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- Among them are spectra of independent samples from 247 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AEP	Prednicarbate, micronized	19E14-B01-191430	3
AHD	Prednicarbate, micronized	1801013-01	1
AHD	Prednicarbate, micronized	1809015-01	1
Caelo	Prednicarbate, micronized	15446303	3
Fagron	Prednicarbate, micronized	15D15-B03-308161	5
Fagron	Prednicarbate, micronized	15D15-B03-308162	1
AHL	Prednicarbate, micronized	16087408	2
Caelo	Prednicarbate, micronized	19122602	3
Anzag	Prednicarbate, micronized	17220408	1
Apomix/Noweda	Prednicarbate, micronized	13372410	2
Bombastus	Prednicarbate, micronized	17220408	1
Bombastus	Prednicarbate, micronized	15446306	1
Fagron	Prednicarbate, micronized	13F11-N01	1
Caelo	Prednicarbate, micronized	16E12-B01	1
Caelo	Prednicarbate, micronized	C0333/1111070	2
Caelo	Prednicarbate, micronized	12383301	1
Caelo	Prednicarbate, micronized	23082013A	1
Caelo	Prednicarbate, micronized	13224401	5
Caelo	Prednicarbate, micronized	13372403	10
Caelo	Prednicarbate, micronized	13372410	6
Caelo	Prednicarbate, micronized	13372411	1
Caelo	Prednicarbate, micronized	15181403	12
Caelo	Prednicarbate, micronized	14J16-B06	3
Caelo	Prednicarbate, micronized	15181411	2
Caelo	Prednicarbate, micronized	2748	1
Caelo	Prednicarbate, micronized	15G10-B02-314082	3
Caelo	Prednicarbate, micronized	15181404	3
Caelo	Prednicarbate, micronized	15446302	11
Caelo	Prednicarbate, micronized	15446305	6
Caelo	Prednicarbate, micronized	2790	1
Caelo	Prednicarbate, micronized	15446304	1
Caelo	Prednicarbate, micronized	160500	1
Caelo	Prednicarbate, micronized	1601058-01	1
Caelo	Prednicarbate, micronized	16087408	17
Caelo	Prednicarbate, micronized	16987410	1
Caelo	Prednicarbate, micronized	16087412	5
Caelo	Prednicarbate, micronized	16087411	3
Caelo	Prednicarbate, micronized	1517E-03595	1
Caelo	Prednicarbate, micronized	15J22-B04-318528	1
Caelo	Prednicarbate, micronized	17014001	3
Caelo	Prednicarbate, micronized	17014005	17
Caelo	Prednicarbate, micronized	1704003	1
Caelo	Prednicarbate, micronized	16J27-B01	1
Caelo	Prednicarbate, micronized	1704005	1
Caelo	Prednicarbate, micronized	16J27-B01-330977	1
Caelo	Prednicarbate, micronized	17220401	5
Caelo	Prednicarbate, micronized	17220407	32
Caelo	Prednicarbate, micronized	1707022-01	3
Caelo	Prednicarbate, micronized	17220406	4
Caelo	Prednicarbate, micronized	17014006	1
Caelo	Prednicarbate, micronized	172204075515	1
Caelo	Prednicarbate, micronized	17315604	25
Caelo	Prednicarbate, micronized	1801013-01	6
Caelo	Prednicarbate, micronized	23051819	1
Caelo	Prednicarbate, micronized	17315609	25
Caelo	Prednicarbate, micronized	17J04-B05-346113	1
Caelo	Prednicarbate, micronized	18194103	6

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Supplier	Substance	Batch	Spectra
Caelo	Prednicarbate, micronized	18194104	26
Caelo	Prednicarbate, micronized	18194112	3
Caelo	Prednicarbate, micronized	18194115	26
Caelo	Prednicarbate, micronized	18197115	1
Caelo	Prednicarbate, micronized	18194117	4
Caelo	Prednicarbate, micronized	19051603	1
Caelo	Prednicarbate, micronized	19051604	4
Caelo	Prednicarbate, micronized	17315606	1
Caelo	Prednicarbate, micronized	17013805	9
Caelo	Prednicarbate, micronized	16E12-B01-325758	1
Caelo	Prednicarbate, micronized	16J27-B01-332958	1
Caelo	Prednicarbate, micronized	18B27-B01-350264	2
Caelo	Prednicarbate, micronized	18194116	2
Caelo	Prednicarbate, micronized	17315605	15
Caelo	Prednicarbate, micronized	19122604	13
Caelo	Prednicarbate, micronized	16087401	13
Caelo	Prednicarbate, micronized	2(18194104)	1
Caelo	Prednicarbate, micronized	3(19051602)	1
Caelo	Prednicarbate, micronized	17J04-B05-343934	1
Caelo	Prednicarbate, micronized	16A18-B01-322732	1
Caelo	Prednicarbate, micronized	16087410	17
Caelo	Prednicarbate, micronized	17220410	2
Caelo	Prednicarbate, micronized	13119401	1
Caelo	Prednicarbate, micronized	13372408	1
Caelo	Prednicarbate, micronized	3267	1
Caelo	Prednicarbate, micronized	3272	1
Caelo	Prednicarbate, micronized	3302	1
Caelo	Prednicarbate, micronized	177220407	1
Caelo	Prednicarbate, micronized	1922604	1
Caelo	Prednicarbate, micronized	15446301	19
Caelo	Prednicarbate, micronized	13372419	5
Caelo	Prednicarbate, micronized	19051601	25
Caelo	Prednicarbate, micronized	12383309	1
Caelo	Prednicarbate, micronized	1507011-01	1
Fagron	Prednicarbate, micronized	NX1422M	2
Caelo	Prednicarbate, micronized	13224406	1
Caelo	Prednicarbate, micronized	15D15-B03	1
Caelo	Prednicarbate, micronized	15D15-B03-310847	2
Caelo	Prednicarbate, micronized	15J22-B-321005	1
Caelo	Prednicarbate, micronized	1608710	1
Caelo	Prednicarbate, micronized	17C27-B01-339079	1
Caelo	Prednicarbate, micronized	15D15-B03-308161	1
Caelo	Prednicarbate, micronized	1607012-01	2
Caelo	Prednicarbate, micronized	17013804	11
Caelo	Prednicarbate, micronized	17315603	5
Caelo	Prednicarbate, micronized	3438	1
Fagron	Prednicarbate, micronized	18194104	1
Caelo	Prednicarbate, micronized	15181409	4
Caelo	Prednicarbate, micronized	17014003	20
Caelo	Prednicarbate, micronized	16J27-B01-330976	1
Caelo	Prednicarbate, micronized	17j04B05346113	1
Caelo	Prednicarbate, micronized	19051602	8
Caelo	Prednicarbate, micronized	19122608	16
Caelo	Prednicarbate, micronized	20000609004	1
Caelo	Prednicarbate, micronized	17220408	31
Caelo	Prednicarbate, micronized	17315607	2
Caelo	Prednicarbate, micronized	18194105	34
Caelo	Prednicarbate, micronized	14A27-B02-295796	1
Caelo	Prednicarbate, micronized	15446306	9
Caelo	Prednicarbate, micronized	16A18-B01-322733	2

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Prednicarbate, micronized	16087410	1
Caesar & Loretz GmbH	Prednicarbate, micronized	18194105	2
Caesar & Loretz GmbH	Prednicarbate, micronized	18194115	5
Caesar & Loretz GmbH	Prednicarbate, micronized	19051601	1
Caesar & Loretz GmbH	Prednicarbate, micronized	19051602	3
Caesar & Loretz GmbH	Prednicarbate, micronized	19122608	1
Caesar & Loretz GmbH	Prednicarbate, micronized	20000609004	2
Caesar & Loretz GmbH / ...	Prednicarbate, micronized	18194112	1
Caesar & Loretz GmbH/Go...	Prednicarbate, micronized	18194117	1
Caesar & Loretz GmbH/Mi...	Prednicarbate, micronized	19051602	1
caesar&lorenz	Prednicarbate, micronized	18149103	1
caesar&lorenz GmbH,AHC,...	Prednicarbate, micronized	16087408	1
Caesar&Loretz GmbH/ San...	Prednicarbate, micronized	19122604	1
caesar&lorenz,Phönix	Prednicarbate, micronized	15181411	1
Caesar/Ebert	Prednicarbate, micronized	18194105	1
Cealo/GEHE	Prednicarbate, micronized	17315609	1
Cealo/Sanacorp	Prednicarbate, micronized	15546306	1
Celo	Prednicarbate, micronized	1687408	1
Defektur	Prednicarbate, micronized	12D27-N04	1
E und J, 22.07.2016	Prednicarbate, micronized	15446306	2
EuRho	Prednicarbate, micronized	1801013-01	1
EuRho/Noweda	Prednicarbate, micronized	1805005-01	1
Euro	Prednicarbate, micronized	1507011-01	1
Euro OTC	Prednicarbate, micronized	1302033-01	1
Euro OTC	Prednicarbate, micronized	1609011-01	1
Euro OTC	Prednicarbate, micronized	13224402	1
Euro OTC	Prednicarbate, micronized	1707022201	1
Euro OTC	Prednicarbate, micronized	180901501	3
Euro OTC	Prednicarbate, micronized	1903023	1
Euro OTC	Prednicarbate, micronized	1805005-01	16
Euro OTC	Prednicarbate, micronized	1609022-01	19
Euro OTC	Prednicarbate, micronized	160902201	1
Euro OTC	Prednicarbate, micronized	160902	1
Euro OTC	Prednicarbate, micronized	1801013-01	27
Euro OTC	Prednicarbate, micronized	17220408	2
Euro OTC	Prednicarbate, micronized	1605001-01	7
Euro OTC	Prednicarbate, micronized	170702201	1
Euro OTC	Prednicarbate, micronized	1805005-02	1
Euro OTC	Prednicarbate, micronized	13372403	1
Euro OTC	Prednicarbate, micronized	1507011-01	2
Euro OTC	Prednicarbate, micronized	19032023-01	1
Euro OTC	Prednicarbate, micronized	1607012-01	8
Euro OTC	Prednicarbate, micronized	1805001-01	2
Euro OTC	Prednicarbate, micronized	1809015-02	1
Euro OTC	Prednicarbate, micronized	1903023-01	11
Euro OTC	Prednicarbate, micronized	1809015-01	22
Euro Pharma/Gehe	Prednicarbate, micronized	1801013-01	1
Euro/Gehe	Prednicarbate, micronized	1609022-01	1
Euro/Gehe	Prednicarbate, micronized	1805005-01	1
Euro/Phönix	Prednicarbate, micronized	1809015-01	2
Euro OTC	Prednicarbate, micronized	1501033-01	2
Euro OTC	Prednicarbate, micronized	1507011-02	4
Euro OTC	Prednicarbate, micronized	1601058-01	5
Euro OTC	Prednicarbate, micronized	1501033-02	4
Euro OTC	Prednicarbate, micronized	1707022-01	31
Euro OTC	Prednicarbate, micronized	180500501	1
Euro OTC	Prednicarbate, micronized	1809015001	1
Fagro/Gehe	Prednicarbate, micronized	15D15-B03-308161	1
Fagron	Prednicarbate, micronized	16E12-B01-325758	5
Fagron	Prednicarbate, micronized	11L23-N07	5

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Supplier	Substance	Batch	Spectra
Fagron	Prednicarbate, micronized	12B20-N06	2
Fagron	Prednicarbate, micronized	13C25-N02	1
Fagron	Prednicarbate, micronized	13C25-N06	6
Fagron	Prednicarbate, micronized	7061303	1
Fagron	Prednicarbate, micronized	13/23-N04	3
Fagron	Prednicarbate, micronized	13I23-N04	1
Fagron	Prednicarbate, micronized	13I23-N04	8
Fagron	Prednicarbate, micronized	8081403	1
Fagron	Prednicarbate, micronized	14A27-B02-291258	2
Fagron	Prednicarbate, micronized	14A27-B02-295796	6
Fagron	Prednicarbate, micronized	14A27-B02-295793	1
Fagron	Prednicarbate, micronized	14J16B06303466	1
Fagron	Prednicarbate, micronized	14J16B06	1
Fagron	Prednicarbate, micronized	14A27-B02	1
Fagron	Prednicarbate, micronized	15D15-B03308161	1
Fagron	Prednicarbate, micronized	2762	1
Fagron	Prednicarbate, micronized	15G10-B02	1
Fagron	Prednicarbate, micronized	15D15-B03-30816	1
Fagron	Prednicarbate, micronized	15G10-B02-311819	1
Fagron	Prednicarbate, micronized	15J22-B04-316799	6
Fagron	Prednicarbate, micronized	15J22-B04-318528	3
Fagron	Prednicarbate, micronized	160518P	1
Fagron	Prednicarbate, micronized	160314PC	1
Fagron	Prednicarbate, micronized	16A18/B01	1
Fagron	Prednicarbate, micronized	16E12-B01-327344	3
Fagron	Prednicarbate, micronized	16J27-B01-330976	9
Fagron	Prednicarbate, micronized	16J27-b01-330976	1
Fagron	Prednicarbate, micronized	16J27-B01-332958	9
Fagron	Prednicarbate, micronized	16j27-b01-330976	1
Fagron	Prednicarbate, micronized	4111706	1
Fagron	Prednicarbate, micronized	17C27-B01-335531	1
Fagron	Prednicarbate, micronized	17220407	2
Fagron	Prednicarbate, micronized	17C27-B01-339079	6
Fagron	Prednicarbate, micronized	17J04-B05-340570	2
Fagron	Prednicarbate, micronized	17J04-B05-341872	7
Fagron	Prednicarbate, micronized	1801013-01	4
Fagron	Prednicarbate, micronized	17j04-b05-343934	1
Fagron	Prednicarbate, micronized	17J04-B05-343934	3
Fagron	Prednicarbate, micronized	17J04-B05-346113	7
Fagron	Prednicarbate, micronized	18B27-B01-347486	14
Fagron	Prednicarbate, micronized	29091807	1
Fagron	Prednicarbate, micronized	18B27-B01-350264	8
Fagron	Prednicarbate, micronized	3251	1
Fagron	Prednicarbate, micronized	18E14B03-352560	1
Fagron	Prednicarbate, micronized	18E14-B03	2
Fagron	Prednicarbate, micronized	18E14-B03-355727	3
Fagron	Prednicarbate, micronized	18194115	1
Fagron	Prednicarbate, micronized	18e14-b03-355726	1
Fagron	Prednicarbate, micronized	18E14-B03-35260	1
Fagron	Prednicarbate, micronized	19E14-B01	1
Fagron	Prednicarbate, micronized	16j27b01330976	1
Fagron	Prednicarbate, micronized	9G14-N06	1
Fagron	Prednicarbate, micronized	13F11-N01	4
Fagron	Prednicarbate, micronized	NW0396M	1
Fagron	Prednicarbate, micronized	18E14-03-352631	1
Fagron	Prednicarbate, micronized	17c27-b01-339079	1
Fagron	Prednicarbate, micronized	15g10-b02-310848	1
Fagron	Prednicarbate, micronized	18B27-B01-346748	2
Fagron	Prednicarbate, micronized	13G05-N03	5
Fagron	Prednicarbate, micronized	16/27-B01-332958	2

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Supplier	Substance	Batch	Spectra
Fagron	Prednicarbate, micronized	14a27-b02-291256	2
Fagron	Prednicarbate, micronized	13F11-No1	1
Fagron	Prednicarbate, micronized	701867-0001	1
Fagron	Prednicarbate, micronized	17J04-B05	1
Fagron	Prednicarbate, micronized	17J04b05-346113	1
Fagron	Prednicarbate, micronized	18B27-B01	1
Fagron	Prednicarbate, micronized	NU0823M	1
Fagron	Prednicarbate, micronized	NU0823M	1
Fagron	Prednicarbate, micronized	15D15-B03-309682	1
Fagron	Prednicarbate, micronized	14A27-B02-295797	7
Fagron	Prednicarbate, micronized	15J22-B04	1
Fagron	Prednicarbate, micronized	19G09-B01	1
Fagron	Prednicarbate, micronized	16A18-B01-322732	4
Fagron	Prednicarbate, micronized	15J-B04-316799	1
Fagron	Prednicarbate, micronized	174J04-B05-343935	1
Fagron	Prednicarbate, micronized	17C27-B01	1
Fagron	Prednicarbate, micronized	9E04-N02	1
Fagron	Prednicarbate, micronized	16E12-B01-328270	3
Fagron	Prednicarbate, micronized	17013804	1
Fagron	Prednicarbate, micronized	17C27-B01-335530	8
Fagron	Prednicarbate, micronized	18B27-01-347486	1
Fagron	Prednicarbate, micronized	18B27-01-350264	1
Fagron	Prednicarbate, micronized	18E14-B03-352631	5
Fagron	Prednicarbate, micronized	NT0780M	2
Fagron	Prednicarbate, micronized	1612-B01-325758	1
Fagron	Prednicarbate, micronized	16E12-B01	2
Fagron	Prednicarbate, micronized	18E14-B03-352560	3
Fagron	Prednicarbate, micronized	13372408	1
Fagron	Prednicarbate, micronized	15J22-B04-318930	2
Fagron	Prednicarbate, micronized	16J27-B01	2
Fagron	Prednicarbate, micronized	19G09-B01-194722	1
Fagron	Prednicarbate, micronized	19J16-B04-197550	1
Fagron	Prednicarbate, micronized	NT0555M13I23-N04	1
Fagron	Prednicarbate, micronized	15G10-B02-310848	8
Fagron	Prednicarbate, micronized	17Jo4B05343934	1
Fagron	Prednicarbate, micronized	15G10-B02-314082	3
Fagron	Prednicarbate, micronized	16E12-B01-330093	2
Fagron	Prednicarbate, micronized	160902201	1
Fagron	Prednicarbate, micronized	15J22-B04-316799	1
Fagron	Prednicarbate, micronized	19E14-B01-191430	1
Fagron	Prednicarbate, micronized	13c25-no6	1
Fagron	Prednicarbate, micronized	17J04-B05-326113	1
Fagron	Prednicarbate, micronized	NX1925M	3
Fagron	Prednicarbate, micronized	18B27-B01-0001	1
Fagron	Prednicarbate, micronized	18B27-B01-351177	1
Fagron	Prednicarbate, micronized	19E14-B01-191431	1
Fagron	Prednicarbate, micronized	16J28-B01-330976	1
Fargon	Prednicarbate, micronized	15J22-B04-318930	1
Fargon	Prednicarbate, micronized	16E12-B01_325758	1
Fargon/Phoenix 05.06.18	Prednicarbate, micronized	17J04-B05-343934	1
Fiebig	Prednicarbate, micronized	17013804	1
Fiebig	Prednicarbate, micronized	17220408	1
Fiebig	Prednicarbate, micronized	18194105	1
Fragron	Prednicarbate, micronized	NV0485M	1
Gehe	Prednicarbate, micronized	12B14-N02	1
Gehe	Prednicarbate, micronized	13G05-n03	1
Gehe	Prednicarbate, micronized	13123-N04	1
Gehe	Prednicarbate, micronized	1707022-01	2
Gehe	Prednicarbate, micronized	1801013-01	5
Gehe	Prednicarbate, micronized	1805005-01	1

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Supplier	Substance	Batch	Spectra
Gehe	Prednicarbate, micronized	1809015-01	4
Gehe	Prednicarbate, micronized	19051601	1
Gehe	Prednicarbate, micronized	1903023-01	2
Gehe	Prednicarbate, micronized	19122604	2
Gehe	Prednicarbate, micronized	19G09-B01-194722	2
Gehe	Prednicarbate, micronized	19G09-B01	1
GEHE	Prednicarbate, micronized	17315607	2
GEHE	Prednicarbate, micronized	7529666	1
GEHE	Prednicarbate, micronized	18194103	4
GEHE	Prednicarbate, micronized	18194116	1
Bombastus	Prednicarbate, micronized	17315605	1
Caelo	Prednicarbate, micronized	1220218/17220407	1
Fagron	Prednicarbate, micronized	10J04-N10	1
Fagron	Prednicarbate, micronized	14J16-B06_303465	1
Hedinger	Prednicarbate, micronized	16J27-B01-330976	2
Hedinger/ Sanacorp	Prednicarbate, micronized	15181403	1
Klenk	Prednicarbate, micronized	17014003	1
Hepart	Prednicarbate, micronized	17C27-B01-335530	1
Jenne	Prednicarbate, micronized	17J04-B05-346113	1
Jenne	Prednicarbate, micronized	18194105	1
Jenne	Prednicarbate, micronized	18194115	2
Jenne	Prednicarbate, micronized	P2019/91	1
JENNE	Prednicarbate, micronized	17220406	2
JENNE	Prednicarbate, micronized	17315603	1
Kehr	Prednicarbate, micronized	16J27-B01-330976	1
Fagron	Prednicarbate, micronized	18B27-B01_347486	1
Fagron	Prednicarbate, micronized	18E14-B03-355726	7
Kriegeram 29.06.2018	Prednicarbate, micronized	17315605	1
Newchem spa/Noweda	Prednicarbate, micronized	14A27-B02-291256	1
Newchem Spa/Sanacorp	Prednicarbate, micronized	16E12-B01	1
Noweda	Prednicarbate, micronized	15446301	1
Noweda	Prednicarbate, micronized	17013804	2
Noweda	Prednicarbate, micronized	1801013-01	1
Noweda	Prednicarbate, micronized	1805005-01	1
Euro OTC	Prednicarbate, micronized	1801013	1
Noweda/Apomix	Prednicarbate, micronized	1609022-01	2
Fagron	Prednicarbate, micronized	14B13-B31-291255	1
Fagron	Prednicarbate, micronized	14J16-B06-303465	14
Euro OTC	Prednicarbate, micronized	1605001	1
Euro OTC	Prednicarbate, micronized	180101301	1
Phoenix	Prednicarbate, micronized	16J27-b01-332958	1
Phoenix	Prednicarbate, micronized	3070	1
Phoenix	Prednicarbate, micronized	17C27-B01-335530	1
Phoenix	Prednicarbate, micronized	3089	1
Phoenix	Prednicarbate, micronized	3097	1
Phoenix	Prednicarbate, micronized	3106	1
Phoenix	Prednicarbate, micronized	3119	1
Phoenix	Prednicarbate, micronized	17315604	3
Phoenix	Prednicarbate, micronized	17315605	1
Phoenix	Prednicarbate, micronized	3208	1
Phoenix	Prednicarbate, micronized	3239	1
Phoenix	Prednicarbate, micronized	3363	1
Phoenix	Prednicarbate, micronized	19122602	1
Phoenix	Prednicarbate, micronized	3408	1
Phoenix 7.02.2020	Prednicarbate, micronized	1903023-01	1
Phönix	Prednicarbate, micronized	16J27-B01-330976	1
Phönix	Prednicarbate, micronized	15J22-B04-318528	1
Phönix	Prednicarbate, micronized	1707022-01	1
Phönix	Prednicarbate, micronized	3134	1
Phönix	Prednicarbate, micronized	3154	1

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Supplier	Substance	Batch	Spectra
Phönix	Prednicarbate, micronized	3185	1
Phönix	Prednicarbate, micronized	18194104	2
Caelo	Prednicarbate, micronized	1213608	1
Sanacorp	Prednicarbate, micronized	11L23-N07	1
Sanacorp	Prednicarbate, micronized	17315604	1
Caelo	Prednicarbate, micronized	13/23-N04	1
Caelo	Prednicarbate, micronized	9764897	1
Fagron	Prednicarbate, micronized	16J27-B01-330977	1
Sanacorp, 01.03.17, 21,...	Prednicarbate, micronized	1687410	1
Sino Phyto	Prednicarbate, micronized	13224401	1
Sonnenberg-Apotheke	Prednicarbate, micronized	1607012-01	1
Caelo	Prednicarbate, micronized	12123610	1
Caelo	Prednicarbate, micronized	1609022-01	3
Caelo	Prednicarbate, micronized		2
Caelo	Prednicarbate, micronized	13119402	2
Euro OTC	Prednicarbate, micronized	1302033-02	2
Euro OTC	Prednicarbate, micronized		1
Fagron	Prednicarbate, micronized	14A27-B02-291256	17
Fagron	Prednicarbate, micronized	12D27-N04	3
Fagron	Prednicarbate, micronized		1

- 109 990 spectra from 742 *Apo-Ident* customers from a total of 31 628 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednicarbate, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednicarbate, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	666	0	110 023
Type B	0	915	0	118 227
Type C	0	1247	10	109 990

The substance/substance group *Prednicarbate, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0991 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.3443 %)
Type C	100.0000 % (> 99.8899 %)	99.2045 % (> 98.9658 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednicarbate, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dexamethasone acetate	19.10	—
Betamethasone valerate	25.69	78.00
Oxybuprocaine hydrochloride	28.60	—
Dexamethasone	29.42	109.31
Methacholine chloride	38.81	—
Triamcinolone acetonide	39.76	46.30
Budesonide, micronized	45.96	91.04
Ciclosporin	51.56	—
⋮	⋮	⋮
Erythromycin	>50	91.94
Prednisolone, micronized	>50	121.13
Norethisterone acetate	>50	127.96
Capsaicin	>50	170.63
Prednisone	>50	179.74
Betamethasone, micronized	>50	252.92
Triamcinolone, micronized	>50	313.84
Heparin sodium	>50	323.12

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednicarbate, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21368	21368	0.00	19.78
25119	25119	0.00	31.06
21610	21610	0.00	19.10
20833	20832	2.09	22.98
22366	22366	0.00	21.58
20832	20832	0.00	22.92
21369	21368	1.76	20.18
21858	21858	0.00	22.79
21572	21572	0.00	28.20
20700	21572	9.21	29.32

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Prednisolon dihydrogen phosphate dinatrium
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20212-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Prednisolon dihydrogen phosphate dinatrium; Prednisoloni natrii phosphas

Special notes

When selecting the *Prednisolon dihydrogen phosphate dinatrium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednisolon dihydrogen phosphate dinatrium	5	2	55

Second-stage model

For differentiation of the substance/substance group *Prednisolon dihydrogen phosphate dinatrium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednisolon dihydrogen phosphate dinatrium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prednisolon dihy...	13304703	20923	40	20130904
Caelo	Prednisolon dihy...	13304704	21412	60	1411052
Caelo	Prednisolon dihy...	16174715	23271	40	20160930
Fagron	Prednisolon dihy...	14E07-B06-295251	21571	60	20140623
Fagron	Prednisolon dihy...	18D23-B08-351348	24293	40	1812421

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Prednisolon dihydrogen phosphate dinatrium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Prednisolon dihydrogen phosphate dinatrium*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prednisolon dihydrogen phosp...	181940	24905	40
Fagron	Prednisolon dihydrogen phosp...	16I14-B03-328918	23270	40
Caelo	Prednisolon dihydrogen phosp...	13304704	21413	60

- 119002 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 115 spectra from 49 *Apo-Ident* customers from 59 batches from the substance/substance group *Prednisolon dihydrogen phosphate dinatrium*.
- Among them are spectra of independent samples from 55 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Alte Apotheke	Prednisolon dihydrogen phosp...	15K27B09-318738	1
Caelo	Prednisolon dihydrogen phosp...	16174701	1
Caelo	Prednisolon dihydrogen phosp...	16174710	1
Caelo	Prednisolon dihydrogen phosp...	18024602	1
Caelo	Prednisolon dihydrogen phosp...	18024604	2
Caelo	Prednisolon dihydrogen phosp...	18194003	2
Caelo	Prednisolon dihydrogen phosp...	18194006	3
Caelo	Prednisolon dihydrogen phosp...	19129302	1
Caelo	Prednisolon dihydrogen phosp...	19275403	1
Caelo	Prednisolon dihydrogen phosp...	17077502	2
Caelo	Prednisolon dihydrogen phosp...	17077508	1
Caelo	Prednisolon dihydrogen phosp...	19129304	1
Caelo	Prednisolon dihydrogen phosp...	15199603	1
Caelo	Prednisolon dihydrogen phosp...	18194001	1
Caelo	Prednisolon dihydrogen phosp...	14196602	1
Caelo	Prednisolon dihydrogen phosp...	16174702	1
Caelo	Prednisolon dihydrogen phosp...	16174706	1
Caelo	Prednisolon dihydrogen phosp...	18194011	1
Caelo	Prednisolon dihydrogen phosp...	15199602	2
Caelo	Prednisolon dihydrogen phosp...	19129306	2
Caesar & Loretz GmbH	Prednisolon dihydrogen phosp...	18194006	1
Fagron	Prednisolon dihydrogen phosp...	11C18-N11	1
Fagron	Prednisolon dihydrogen phosp...	12H30-N08	2
Fagron	Prednisolon dihydrogen phosp...	13A10-N04	3
Fagron	Prednisolon dihydrogen phosp...	13C26N06	1
Fagron	Prednisolon dihydrogen phosp...	13H19N04	1
Fagron	Prednisolon dihydrogen phosp...	14E07-B06-295253	1
Fagron	Prednisolon dihydrogen phosp...	14G30-B09-303014	4
Fagron	Prednisolon dihydrogen phosp...	NU1356	1
Fagron	Prednisolon dihydrogen phosp...	15J01-B02-313610	2
Fagron	Prednisolon dihydrogen phosp...	15J01-B02-312722	5
Fagron	Prednisolon dihydrogen phosp...	15J01-B02	4
Fagron	Prednisolon dihydrogen phosp...	15K27-B09-318738	2
Fagron	Prednisolon dihydrogen phosp...	15K27-B09	4
Fagron	Prednisolon dihydrogen phosp...	15K27-B09-322162	1

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Supplier	Substance	Batch	Spectra
Fagron	Prednisolon dihydrogen phosp...	PSP002/0816	2
Fagron	Prednisolon dihydrogen phosp...	16I14-B03	2
Fagron	Prednisolon dihydrogen phosp...	13/27-N01	1
Fagron	Prednisolon dihydrogen phosp...	14g30-b09-303014	1
Fagron	Prednisolon dihydrogen phosp...	15k27-b09-318738	1
Fagron	Prednisolon dihydrogen phosp...	17/27-b03-342560	1
Fagron	Prednisolon dihydrogen phosp...	15K27-B09-322163	3
Fagron	Prednisolon dihydrogen phosp...	17B08-B05-337466	3
Fagron	Prednisolon dihydrogen phosp...	17I27-B03-345405	1
Fagron	Prednisolon dihydrogen phosp...	17I27-B03	2
Fagron	Prednisolon dihydrogen phosp...	11K11-N11	2
Fagron	Prednisolon dihydrogen phosp...	15F29-B11-309694	1
Fagron	Prednisolon dihydrogen phosp...	17B08B05337466	1
Fagron	Prednisolon dihydrogen phosp...	15f29-b11-309694	1
Fagron	Prednisolon dihydrogen phosp...	14G30-B09-303012	6
Fagron	Prednisolon dihydrogen phosp...	15J01-B02-317180	2
Fagron	Prednisolon dihydrogen phosp...	15K27-B09-326263	3
Fagron	Prednisolon dihydrogen phosp...	16I14-B03-328918	2
Fagron	Prednisolon dihydrogen phosp...	14G30-B09	1
Fagron	Prednisolon dihydrogen phosp...	15K27B09-326263	1
Fagron	Prednisolon dihydrogen phosp...	16/14-B03-328169	1
Fagron	Prednisolon dihydrogen phosp...	13I27-N01	3
Fagron	Prednisolon dihydrogen phosp...	17I27-B03-344246	1
Newchem spa	Prednisolon dihydrogen phosp...	15J01-B02-313610	2
Sidonia	Prednisolon dihydrogen phosp...	17I27-B03-344246	1
Sidonia	Prednisolon dihydrogen phosp...	17I27-B03-345405	6
Sidonia	Prednisolon dihydrogen phosp...	17I27-B03-342560	1
Fagron	Prednisolon dihydrogen phosp...	14E07-B06-295251	3

- 111 132 spectra from 742 *Apo-Ident* customers from a total of 31 833 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednisolon dihydrogen phosphate dinatrium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednisolon dihydrogen phosphate dinatrium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	237	3	110 449
Type B	0	140	0	119 002
Type C	0	115	0	111 132

The substance/substance group *Prednisolon dihydrogen phosphate dinatrium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	98.7500 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 94.7826 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednisolon dihydrogen phosphate dinatrium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cyanocobalamin	19.28	—
Methylprednisolone	22.40	—
Dexamethasone	28.41	—
Bacitracin	31.18	—
Magnesium citrate	42.96	—
Prednisone	44.36	—
Prednisolone acetate	45.94	—
Dexamethasone acetate	47.32	—
L-glutathione	48.68	—
Estriol	49.19	—
Minoxidil	49.60	—
Triamcinolone, micronized	50.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednisolon dihydrogen phosphate dinatrium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24293	24293	0.00	19.28
20923	21412	7.59	30.42
21412	21412	0.00	28.41
21571	21412	7.02	39.41
23271	21412	9.68	39.28

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prednisolone acetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20089-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prednisolone acetate; Prednisoloni acetas

Special notes

When selecting the *Prednisolone acetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednisolone acetate	8	6	257

Second-stage model

For differentiation of the substance/substance group *Prednisolone acetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednisolone acetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prednisolone ace...	12091814	20784	80	20120416
Caelo	Prednisolone ace...	12324502	20877	40	20121112
Caelo	Prednisolone ace...	13262605	21448	60	20130923
Caelo	Prednisolone ace...	13262605	21450	60	20130923
Caelo	Prednisolone ace...	13262605	21450SI	47	20130923
Euro OTC	Prednisolone ace...	1306040	21096	40	20130812
Euro OTC	Prednisolone ace...	1209028-03	21530	60	AR-15-FG-010480-01
Euro OTC	Prednisolone ace...	1512020	22297	45	20160119*
Euro OTC	Prednisolone ace...	1512020	22297SI	44	20160119*
Fagron	Prednisolone ace...	12H14-N07	20795	40	20120829
Fagron	Prednisolone ace...	12H14-N07	20795SI	49	20120829
Fagron	Prednisolone ace...	15I23-B04-345785	24587	40	20151014

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 605 spectra of 12 reference samples from the substance/substance group *Prednisolone acetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 084 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 588 spectra of 14 reference samples from the substance/substance group *Prednisolone acetate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prednisolone acetate	180673	24534	40
Euro OTC	Prednisolone acetate	1607010	22710	40
Euro OTC	Prednisolone acetate	1701041	23142	40
Euro OTC	Prednisolone acetate	1805009	24133	40
Euro OTC	Prednisolone acetate	1903031	24636	40
Euro OTC	Prednisolone acetate	1911014	24960	40
Caelo	Prednisolone acetate	13262605	21448SI [†]	44
Caelo	Prednisolone acetate	180673	24534SI	80
Euro OTC	Prednisolone acetate	1607010	22710SI	40
Euro OTC	Prednisolone acetate	1701041	23142SI	24
Euro OTC	Prednisolone acetate	1805009	24133SI	40
Euro OTC	Prednisolone acetate	1903031	24636SI	40
Euro OTC	Prednisolone acetate	1911014	24960SI	40
Fagron	Prednisolone acetate	15I23-B04-345785	24587SI [†]	40

- 118 554 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1576 spectra from 508 *Apo-Ident* customers from 269 batches from the substance/substance group *Prednisolone acetate*.
- Among them are spectra of independent samples from 256 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H. 23.05.13 ek: 5,40EUR	Prednisolone acetate	13A07-N07	1
A.H.D.	Prednisolone acetate	14175514	1
Caelo	Prednisolone acetate	16248808	1
AHD 06.03.15	Prednisolone acetate	14175508	1
AHD 23.10.14 EK17,24	Prednisolone acetate	13262601	1
Alliance	Prednisolone acetate	1209028-02	2
Alliance Healthcare	Prednisolone acetate	12091807	1
AllianceHealthcare	Prednisolone acetate	15055201	1
Anzag	Prednisolone acetate	13A07N07	1
Anzag	Prednisolone acetate	16246812	1
ANZAG	Prednisolone acetate	12091802	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
apo-ident	Prednisolone acetate	1512020-01	1
Beiersdorf AG	Prednisolone acetate	15055201	1
Beiersdorf AG	Prednisolone acetate	15398302	1
Bombastus	Prednisolone acetate	17185601	1
Caesar/Loretz,Fa.Gehe	Prednisolone acetate	14380910	1
Cael Sanacorp 05.02.2016	Prednisolone acetate	14380901	1
Cael Sanacorp 05.02.2016	Prednisolone acetate	14175509	1
Caelo	Prednisolone acetate	11158003	1
Caelo	Prednisolone acetate	12091802	6
Caelo	Prednisolone acetate	12091804	8
Caelo	Prednisolone acetate	6021306	1
Caelo	Prednisolone acetate	12091806	3
Caelo	Prednisolone acetate	12091815	2
Caelo	Prednisolone acetate	11080403	1
Caelo	Prednisolone acetate	12324506	11
Caelo	Prednisolone acetate	13262601	16
Caelo	Prednisolone acetate	27051301	1
Caelo	Prednisolone acetate	1306040-01	1
Caelo	Prednisolone acetate	13262603	8
Caelo	Prednisolone acetate	13262606	4
Caelo	Prednisolone acetate	12324514	5
Caelo	Prednisolone acetate	5031511	1
Caelo	Prednisolone acetate	15055201	9
Caelo	Prednisolone acetate	15055202	16
Caelo	Prednisolone acetate	8699	1
Caelo	Prednisolone acetate	14380302	1
Caelo	Prednisolone acetate	1480905	1
Caelo	Prednisolone acetate	14380904	2
Caelo	Prednisolone acetate	15398304	7
Caelo	Prednisolone acetate	15398303	10
Caelo	Prednisolone acetate	15398306	5
Caelo	Prednisolone acetate	15398408	10
Caelo	Prednisolone acetate	15398402	14
Caelo	Prednisolone acetate	15398407	8
Caelo	Prednisolone acetate	15396304	1
Caelo	Prednisolone acetate	16246803	14
Caelo	Prednisolone acetate	160701001	3
Caelo	Prednisolone acetate	165246802	1
Caelo	Prednisolone acetate	162468	2
Caelo	Prednisolone acetate	16246808	12
Caelo	Prednisolone acetate	1624806	1
Caelo	Prednisolone acetate	17086103	12
Caelo	Prednisolone acetate	17086102	9
Caelo	Prednisolone acetate	17086104	13
Caelo	Prednisolone acetate	17185602	15
Caelo	Prednisolone acetate	1701041-01	1
Caelo	Prednisolone acetate	17086101	15
Caelo	Prednisolone acetate	13121715	1
Caelo	Prednisolone acetate	1701041-02	4
Caelo	Prednisolone acetate	170861015494	1
Caelo	Prednisolone acetate	18004401	16
Caelo	Prednisolone acetate	17041802	1
Caelo	Prednisolone acetate	23051812	1
Caelo	Prednisolone acetate	21071808	1
Caelo	Prednisolone acetate	18004903	1
Caelo	Prednisolone acetate	18004403	1
Caelo	Prednisolone acetate	18067303	14
Caelo	Prednisolone acetate	18067309	18
Caelo	Prednisolone acetate	18398303	1
Caelo	Prednisolone acetate	26011905	1

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Supplier	Substance	Batch	Spectra
Caelo	Prednisolone acetate	18067314	8
Caelo	Prednisolone acetate	18067317	10
Caelo	Prednisolone acetate	1867314	1
Caelo	Prednisolone acetate	18067325	1
Caelo	Prednisolone acetate	18067324	7
Caelo	Prednisolone acetate	11158002	1
Caelo	Prednisolone acetate	80673201	1
Caelo	Prednisolone acetate	15055203	2
Caelo	Prednisolone acetate	16246806	8
Caelo	Prednisolone acetate	1475509	1
Caelo	Prednisolone acetate	17185601	20
Caelo	Prednisolone acetate	192969003	1
Caelo	Prednisolone acetate	16246805	2
Caelo	Prednisolone acetate	1234506	1
Caelo	Prednisolone acetate	15398307	10
Caelo	Prednisolone acetate	17086106	2
Caelo	Prednisolone acetate	13262609	3
Caelo	Prednisolone acetate	14380910	10
Caelo	Prednisolone acetate	313I-02106	1
Caelo	Prednisolone acetate	11L21-N03	1
Caelo	Prednisolone acetate	12091813	1
Caelo	Prednisolone acetate	1209028-02	2
Caelo	Prednisolone acetate	20160727Ma1	1
Caelo	Prednisolone acetate	18067309-P20180115Ma	1
Caelo	Prednisolone acetate	15398401	9
Caelo	Prednisolone acetate	18067320	8
Caelo	Prednisolone acetate	14175512	1
Caelo	Prednisolone acetate	17185604	4
Caelo	Prednisolone acetate	12324503	1
Caelo	Prednisolone acetate	18067302	16
Caelo	Prednisolone acetate	18067310	9
Caelo	Prednisolone acetate	717Q-02106	1
Caelo	Prednisolone acetate	12091807	5
Caelo	Prednisolone acetate	12324504	6
Caelo	Prednisolone acetate	12091808	4
Caelo	Prednisolone acetate	1616I-02106	1
Caelo	Prednisolone acetate	14175514	7
Caelo	Prednisolone acetate	16246807	12
Caelo	Prednisolone acetate	171856010	1
Caelo	Prednisolone acetate	16246802	9
Caelo	Prednisolone acetate	12L05-N01	1
Caelo	Prednisolone acetate	13343112	1
Caelo	Prednisolone acetate	14175509	8
Caelo	Prednisolone acetate	1512020-01	4
Caelo	Prednisolone acetate	16246812	7
Caelo	Prednisolone acetate	16246809	2
Caelo	Prednisolone acetate	15B03B05302564	1
Caelo	Prednisolone acetate	12324508	9
Caelo	Prednisolone acetate	14380903	2
Caelo	Prednisolone acetate	151202001	1
Caelo	Prednisolone acetate	16246811	8
Caelo	Prednisolone acetate	170104101	2
Fagron	Prednisolone acetate	1805009-01	1
Caelo	Prednisolone acetate	13262602	8
Caelo	Prednisolone acetate	14175513	10
Caelo	Prednisolone acetate	4313A-02106	1
Caelo	Prednisolone acetate	1406014-01	2
Caelo	Prednisolone acetate	14380909	14
Caelo	Prednisolone acetate	15344002	1
Caelo	Prednisolone acetate	16246801	16

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Supplier	Substance	Batch	Spectra
Caelo	Prednisolone acetate	17086105	10
Caelo	Prednisolone acetate	18004402	11
Caelo	Prednisolone acetate	18067323	1
Caelo	Prednisolone acetate	18067316	1
Caelo	Prednisolone acetate	14380902	13
Caelo	Prednisolone acetate	1306040-02	1
Caelo	Prednisolone acetate	15398302	12
Caelo	Prednisolone acetate	1607010-01	6
Caelo	Prednisolone acetate	16246804	11
Caelo	Prednisolone acetate	1805009-01	2
Caelo	Prednisolone acetate	180673025724	1
Caelo	Prednisolone acetate	12091803	3
Caelo	Prednisolone acetate	12091810	2
Caelo	Prednisolone acetate	12324509	2
Caelo	Prednisolone acetate	14175508	14
Caelo	Prednisolone acetate	14380901	15
Caelo	Prednisolone acetate	15055206	9
Caelo	Prednisolone acetate	14380905	16
Caelo	Prednisolone acetate	1624801	1
Caelo	Prednisolone acetate	17185603	21
Caelo	Prednisolone acetate	32304015	1
Caelo	Prednisolone acetate	162446808	1
Caelo	Prednisolone acetate	180500903	1
Caelo	Prednisolone acetate	1805009-02	1
Caesar & Loretz GmbH	Prednisolone acetate	18067307	3
Caesar & Loretz GmbH	Prednisolone acetate	18067314	1
Caesar & Loretz GmbH	Prednisolone acetate	18067310	1
Caesar & Loretz GmbH	Prednisolone acetate	18067317	2
Caesar & Loretz GmbH	Prednisolone acetate	18067320	1
Caesar & Loretz GmbH	Prednisolone acetate	18067323	1
Caesar & Loretz GmbH	Prednisolone acetate	192969002	1
Caesar & Loretz GmbH / ...	Prednisolone acetate	17185603	1
Caesar & Loretz GmbH, P...	Prednisolone acetate	17086105	1
Caesar & Loretz GmbH, P...	Prednisolone acetate	17185601	1
caesar&lorenz	Prednisolone acetate	14380909	1
Caesar&Loretz GmbH	Prednisolone acetate	15396408	1
Caesar&Loretz GmbH,PHön...	Prednisolone acetate	17086103	2
Caesar&lorenz,AHC,29.08...	Prednisolone acetate	15398306	1
Caesar&lorenz,Phoenix	Prednisolone acetate	13262606	1
Caesar&lorenz,Phoenix	Prednisolone acetate	14175513	1
caesar&lorenz,Phönix	Prednisolone acetate	15055202	2
Caesar&Loretz,Phönix,08...	Prednisolone acetate	15398302	1
Caesar&LoretzGmbH,11.03...	Prednisolone acetate	16246803	1
Cealo	Prednisolone acetate	14175513	1
Ceasar & Loretz GmbH, P...	Prednisolone acetate	18067303	1
Delta	Prednisolone acetate	17086103	1
Delta	Prednisolone acetate	17185602	1
Delta	Prednisolone acetate	18067314	1
Eurho	Prednisolone acetate	1701041-01	2
EuRho	Prednisolone acetate	1306040-03	1
EuRho	Prednisolone acetate	1512020-01	1
EuRho	Prednisolone acetate	1701041-02	1
EuRho	Prednisolone acetate	1701041-01	1
EuRho	Prednisolone acetate	170104102	1
EuRho	Prednisolone acetate	1406014-02	1
EuRho	Prednisolone acetate	1805009-01	2
EuRho	Prednisolone acetate	1805009-02	1
EuRho / Fiebig	Prednisolone acetate	1903031-01	1
EuRho/Noweda	Prednisolone acetate	18004401	1
Euro OTC	Prednisolone acetate	1607010-10	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Prednisolone acetate	711212106	1
Euro OTC	Prednisolone acetate	2413Q02106	1
Euro OTC	Prednisolone acetate	1209028	1
Euro OTC	Prednisolone acetate	1406014-01	15
Euro OTC	Prednisolone acetate	13262606	1
Euro OTC	Prednisolone acetate	1406014-02	12
Euro OTC	Prednisolone acetate	150103601	3
Euro OTC	Prednisolone acetate	1501036-02	32
Euro OTC	Prednisolone acetate	1512020-01	32
Euro OTC	Prednisolone acetate	161005PA	1
Euro OTC	Prednisolone acetate	170104101	2
Euro OTC	Prednisolone acetate	18004403	1
Euro OTC	Prednisolone acetate	1701041	1
Euro OTC	Prednisolone acetate	170413PA/1607010-01	1
Euro OTC	Prednisolone acetate	1701041-01	32
Euro OTC	Prednisolone acetate	1805009-02	15
Euro OTC	Prednisolone acetate	1306040-01	22
Euro OTC	Prednisolone acetate	1460614-01	1
Euro OTC	Prednisolone acetate	K07D20161003M	1
Euro OTC	Prednisolone acetate	1306040-02	14
Euro OTC	Prednisolone acetate	1306040-1	1
Euro OTC	Prednisolone acetate	130604002	1
Euro OTC	Prednisolone acetate	1406012-02	1
Euro OTC	Prednisolone acetate	1501036-01	20
Euro OTC	Prednisolone acetate	K07A20140304M	1
Euro OTC	Prednisolone acetate	1701041-02	29
Euro OTC	Prednisolone acetate	1209028-01	3
Euro OTC	Prednisolone acetate	1108043-02	11
Euro OTC	Prednisolone acetate	1805009-01	32
Euro OTC	Prednisolone acetate	2(1903031-01)	1
Euro OTC	Prednisolone acetate	514U2106	1
Euro OTC	Prednisolone acetate	1203028-03	1
Euro OTC	Prednisolone acetate	18067320	1
Euro OTC	Prednisolone acetate	1209028-02	11
Euro OTC	Prednisolone acetate	18067302	1
Euro OTC	Prednisolone acetate	1911014-01	1
Euro OTC	Prednisolone acetate	1108043-01	2
Euro OTC	Prednisolone acetate	289295	1
Euro OTC	Prednisolone acetate	150103602	1
Euro OTC	Prednisolone acetate	160701001	2
Euro OTC	Prednisolone acetate	5012I-02106	1
Euro OTC	Prednisolone acetate	2714U-02106	1
Euro OTC	Prednisolone acetate	2215I-02106	1
Euro OTC	Prednisolone acetate	1701041-03	5
Euro OTC	Prednisolone acetate	170104-02	1
Euro OTC	Prednisolone acetate	1805009	3
Euro OTC	Prednisolone acetate	1903031-01	16
Euro OTC	Prednisolone acetate	1501036	1
Euro OTC	Prednisolone acetate	1607010-01	89
Euro OTC	Prednisolone acetate	1805009-03	4
EUro/AHD	Prednisolone acetate	1306040-01	1
EUro/AHD	Prednisolone acetate	1306040-02	1
Euro/Phönix	Prednisolone acetate	1805009-02	1
Euroo/Gehe	Prednisolone acetate	1501036-02	1
Euro OTC	Prednisolone acetate	200540	2
Euro OTC	Prednisolone acetate	1903031-02	1
Euro OTC	Prednisolone acetate	170104102	1
Fagron	Prednisolone acetate	12h14-n07	1
Fagron	Prednisolone acetate	12C19-N03	4
Fagron	Prednisolone acetate	11I09N-08	1

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Supplier	Substance	Batch	Spectra
Fagron	Prednisolone acetate	11I09-N08	1
Fagron	Prednisolone acetate	12G25-N05	5
Fagron	Prednisolone acetate	11A31-N03	1
Fagron	Prednisolone acetate	12H14-N07	1
Fagron	Prednisolone acetate	113Q-02106	1
Fagron	Prednisolone acetate	12J10-N05	1
Fagron	Prednisolone acetate	12L05-N01	5
Fagron	Prednisolone acetate	12324502	1
Fagron	Prednisolone acetate	13a07n07	1
Fagron	Prednisolone acetate	13A07-N07	7
Fagron	Prednisolone acetate	6082013D	1
Fagron	Prednisolone acetate	12J10/N05	1
Fagron	Prednisolone acetate	12L11-B40-286915	2
Fagron	Prednisolone acetate	13262605	1
Fagron	Prednisolone acetate	13K20-B04-289495	3
Fagron	Prednisolone acetate	12L11-B04-286905	1
Fagron	Prednisolone acetate	12k20-b04293971	1
Fagron	Prednisolone acetate	14D04-B03-299294	4
Fagron	Prednisolone acetate	13K20-B04-293970	1
Fagron	Prednisolone acetate	14G30-B13-302562	1
Fagron	Prednisolone acetate	14D04B03299295	1
Fagron	Prednisolone acetate	15B03-B05-308582	3
Fagron	Prednisolone acetate	15803-B05	1
Fagron	Prednisolone acetate	15b03-b05-302564	1
Fagron	Prednisolone acetate	15F29-B07-321001	2
Fagron	Prednisolone acetate	15B03B05302564	1
Fagron	Prednisolone acetate	15I23-B04-331154	3
Fagron	Prednisolone acetate	15I23-B04-327929	1
Fagron	Prednisolone acetate	15F29-B07-323268	1
Fagron	Prednisolone acetate	15B03-B05	1
Fagron	Prednisolone acetate	5444	1
Fagron	Prednisolone acetate	1523-B04	1
Fagron	Prednisolone acetate	17189601	1
Fagron	Prednisolone acetate	15I23-B04-340335	1
Fagron	Prednisolone acetate	15I23-B04-341793	1
Fagron	Prednisolone acetate	15/23-B04-341793	1
Fagron	Prednisolone acetate	15I23-B04-341793	2
Fagron	Prednisolone acetate	15B03_B05_302564	2
Fagron	Prednisolone acetate	12C19-N03	1
Fagron	Prednisolone acetate	13D03-N06	1
Fagron	Prednisolone acetate	15/23-B04-334702	1
Fagron	Prednisolone acetate	14G30-B13-299293	2
Fagron	Prednisolone acetate	13K20-B04-289494	2
Fagron	Prednisolone acetate	13K20-B04-293971	3
Fagron	Prednisolone acetate	15/23-B04-334688	1
Fagron	Prednisolone acetate	15i23-b04-336299	1
Fagron	Prednisolone acetate	15I23-B04-336299	2
Fagron	Prednisolone acetate	180713a	1
Fagron	Prednisolone acetate	K07A20130903M	1
Fagron	Prednisolone acetate	15B03-B05-302564	14
Fagron	Prednisolone acetate	15398401	1
Fagron	Prednisolone acetate	K07D20150105M	2
Fagron	Prednisolone acetate	15I23-B4-334688	1
Fagron	Prednisolone acetate	115B03-B05-308582	1
Fagron	Prednisolone acetate	14G30-B13	1
Fagron	Prednisolone acetate	15F29-B07-317179	1
Fagron	Prednisolone acetate	1607010-01	1
Fagron	Prednisolone acetate	15I23-B04-334702	1
Fagron	Prednisolone acetate	12L11-B40-286905	13
Fagron	Prednisolone acetate	12L11-B40	1

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Supplier	Substance	Batch	Spectra
Fagron	Prednisolone acetate	15B03-B05-302566	1
Fargo	Prednisolone acetate	12025-N05	1
Fargon	Prednisolone acetate	13A07-N07	1
Fiebig	Prednisolone acetate	1501036-01	1
Fiebig	Prednisolone acetate	18067307	1
Fiebig	Prednisolone acetate	18067317	1
Finteler Apotheke	Prednisolone acetate	16246812	1
Finteler Apotheke	Prednisolone acetate	17086103	1
Fragron	Prednisolone acetate	K07A20131101M	1
Gehe	Prednisolone acetate	12H14-N07	1
Gehe	Prednisolone acetate	1209028-02	2
Gehe	Prednisolone acetate	1209028-01	1
Gehe	Prednisolone acetate	1406014-01	1
Gehe	Prednisolone acetate	13262609	1
Gehe	Prednisolone acetate	16246806	2
Gehe	Prednisolone acetate	16246803	2
Gehe	Prednisolone acetate	1701041-02	1
Gehe	Prednisolone acetate	1805009-03	1
Gehe	Prednisolone acetate	1911014-01	1
GEHE	Prednisolone acetate	16246807	1
GEHE	Prednisolone acetate	17185601	1
GEHE	Prednisolone acetate	18067302	1
GEHE	Prednisolone acetate	1903031-01	1
GEHE 03.07.2014	Prednisolone acetate	13262605	1
Bombastus	Prednisolone acetate	2255	1
Caelo	Prednisolone acetate	17086103/1110917	1
Gehe/EuRo	Prednisolone acetate	1701041-02	1
Euro OTC	Prednisolone acetate	190303101	1
Henan Lihua Pharmaceuti...	Prednisolone acetate	14G30-B13	1
Kehr	Prednisolone acetate	1406014-01	1
L12/Apomix	Prednisolone acetate	16246804	1
L30	Prednisolone acetate	18004402	1
L30	Prednisolone acetate	18067303	1
Lihua Pharm	Prednisolone acetate	K07A20140302M	1
Lihua Pharma	Prednisolone acetate	1406014-01	1
noweda	Prednisolone acetate	14175513	1
Noweda	Prednisolone acetate	1209028-01	1
Noweda	Prednisolone acetate	12324506	1
Noweda	Prednisolone acetate	12L11-B40-286905	1
Noweda	Prednisolone acetate	15055202	1
Noweda	Prednisolone acetate	15398303	1
Noweda	Prednisolone acetate	K07D20150105M	1
Noweda	Prednisolone acetate	1523-B04-334688	1
Noweda	Prednisolone acetate	17010410203707556	1
Noweda	Prednisolone acetate	1701041-02	1
Caelo	Prednisolone acetate	1406014-02	2
Noweda 18.05.2015	Prednisolone acetate	14D04-B03-299294	1
Noweda/EuRo	Prednisolone acetate	1607010-01	1
Euro OTC	Prednisolone acetate	1306040-03	1
Euro OTC	Prednisolone acetate	2507212106	1
Euro OTC	Prednisolone acetate	151202001	1
Phoenix	Prednisolone acetate	12L11-B40-286905	1
Phoenix	Prednisolone acetate	14380905	1
Phoenix	Prednisolone acetate	17185602	2
Phoenix	Prednisolone acetate	18067310	1
Phoenix	Prednisolone acetate	3369	1
Phoenix	Prednisolone acetate	192969004	1
Caelo	Prednisolone acetate	1903031-01	1
Fagron	Prednisolone acetate	200540-0013	1
phönix	Prednisolone acetate	1512020-01	1

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Supplier	Substance	Batch	Spectra
phönix	Prednisolone acetate	14380902	2
phönix	Prednisolone acetate	14380910	1
phönix	Prednisolone acetate	15398303	1
phönix	Prednisolone acetate	15398402	1
phönix	Prednisolone acetate	1438910	1
phönix	Prednisolone acetate	16246803	3
phönix	Prednisolone acetate	16246806	1
phönix	Prednisolone acetate	16246807	1
Phönix	Prednisolone acetate	11158008	1
Phönix	Prednisolone acetate	1209028-02	1
Phönix	Prednisolone acetate	12324506	1
Phönix	Prednisolone acetate	13262605	2
Phönix	Prednisolone acetate	16246804	1
Phönix	Prednisolone acetate	15398303	1
Phönix	Prednisolone acetate	17185602	1
Phönix	Prednisolone acetate	18067303	1
Phönix	Prednisolone acetate	18067317	1
Caelo	Prednisolone acetate	18067307	11
Phönix 09.05.2019	Prednisolone acetate	1805009-02	1
Phönix 23.08.2019	Prednisolone acetate	18067320	1
Caelo	Prednisolone acetate	18067308	3
Phönix W.E:17.03.18 E...	Prednisolone acetate	17185601	1
Phönix _28.11.2018	Prednisolone acetate	1805009-01	2
PhönixWE:10.02.2017 E...	Prednisolone acetate	16246806	1
Sana	Prednisolone acetate	15L23B04345785	1
sanacorp	Prednisolone acetate	14380909	1
Sanacorp	Prednisolone acetate	12091808	1
Sanacorp	Prednisolone acetate	15055206	1
Sanacorp	Prednisolone acetate	15398408	1
Sanacorp	Prednisolone acetate	17086104	1
Sanacorp	Prednisolone acetate	17185601	1
Sanacorp	Prednisolone acetate	15123-B04-341793	1
Sanacorp	Prednisolone acetate	17185602	1
Sanacorp	Prednisolone acetate	15123-B04-334688	2
Sanacorp	Prednisolone acetate	18067303	2
Caelo	Prednisolone acetate	32304	1
Caelo	Prednisolone acetate	12324505	16
Caelo	Prednisolone acetate	16/AKD2	1
Caelo	Prednisolone acetate	18067301	4
Spangro 08.05.2018	Prednisolone acetate	17185601	1
Spangro 30.5.14	Prednisolone acetate	13262606	1
Symbiotica Spec./Phönix	Prednisolone acetate	1306040-02	1
Symbiotika/Anzag	Prednisolone acetate	1306040-01	1
VDL;7,15EUR, 21:06:14	Prednisolone acetate	13262602	1
Wolf-Apotheke	Prednisolone acetate	14380911	1
	Prednisolone acetate	15398303	1
Caelo	Prednisolone acetate	13262605	12
Caelo	Prednisolone acetate	12091814	7
Caelo	Prednisolone acetate	12324502	12
Caesar&lorenz,Phoenix,2...	Prednisolone acetate		1
Euro OTC	Prednisolone acetate	1209028-03	2
Euro OTC	Prednisolone acetate		1
Fagron	Prednisolone acetate	12H14-N07	4
Fagron	Prednisolone acetate		1
Caelo	Prednisolone acetate		2

- 109 671 spectra from 742 *Apo-Ident* customers from a total of 31 630 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are docu-

mented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednisolone acetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednisolone acetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	605	0	110 084
Type B	0	588	0	118 554
Type C	0	1542	34	109 671

The substance/substance group *Prednisolone acetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0083 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.9796 %)
Type C	100.0000 % (> 99.8899 %)	97.8426 % (> 97.6523 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednisolone acetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisone	28.85	—
Gramicidin	49.64	—
Magnesium citrate	51.69	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednisolone acetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20795	22297	4.77	32.80
21096	21530	3.70	34.38
21450	22297	5.01	31.30
20877	22297	3.93	34.37
21530	21530	0.00	32.61
22297	22297	0.00	32.46
20784	22297	4.44	36.16
24587	22297	8.71	31.15
21448	21530	3.53	32.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prednisolone hydrogen succinate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20838-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prednisolone hydrogen succinate; Prednisoloni hydrogenosuccinas

Special notes

When selecting the *Prednisolone hydrogen succinate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednisolone hydrogen succinate	2	2	9

Second-stage model

For differentiation of the substance/substance group *Prednisolone hydrogen succinate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednisolone hydrogen succinate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Prednisolone hyd...	13D16-N11	20956	40	1509250
Fagron	Prednisolone hyd...	14G29-B07-304733	22652	40	1701370
Fagron	Prednisolone hyd...	14G29-B07-304733	22723	40	20140825

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Prednisolone hydrogen succinate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 569 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Prednisolone hydrogen succinate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Prednisolone hydrogen succin...	12A20-N11	20838	40
Fagron	Prednisolone hydrogen succin...	15C11-B05-344778	24058	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 9 *Apo-Ident* customers from 10 batches from the substance/substance group *Prednisolone hydrogen succinate*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Prednisolone hydrogen succin...	15C11B05328275	1
Caelo	Prednisolone hydrogen succin...	12A20-N11	1
Caelo	Prednisolone hydrogen succin...	19081502	1
Caelo	Prednisolone hydrogen succin...	15C11-B05-305533	1
Fagron	Prednisolone hydrogen succin...	15C11-B05-338297	1
Fagron	Prednisolone hydrogen succin...	15C11-B05-344778	3
Fagron	Prednisolone hydrogen succin...	12L14-N04	1
Phönix	Prednisolone hydrogen succin...	13H24-N04	1
Fagron	Prednisolone hydrogen succin...	15c11-B05338297	1
Fagron	Prednisolone hydrogen succin...	14G29-B07-304733	1

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 881 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednisolone hydrogen succinate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednisolone hydrogen succinate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	80	0	119 062
Type C	0	12	0	111 235

The substance/substance group *Prednisolone hydrogen succinate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednisolone hydrogen succinate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Naloxone hydrochloride dihydrate	26.53	—
Prednisolon dihydrogen phosphate dinat...	28.70	—
Dexamethasone acetate	38.72	—
Triamcinolone acetonide	43.31	—
Clobetasol propionate	45.47	—
Dexamethasone	45.81	—
Estriol	49.21	—
Sodium edetate	52.37	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednisolone hydrogen succinate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20956	20956	0.00	38.72
22652	22652	0.00	39.70
22723	22652	1.00	38.81

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prednisolone, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20773-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prednisolone, micronized; Prednisolonum micronisatum

Special notes

When selecting the *Prednisolone, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednisolone, micronized	12	5	275

Second-stage model

For differentiation of the substance/substance group *Prednisolone, micronized* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednisolone, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prednisolone, mi...	12324202	20773	40	20121113
Caelo	Prednisolone, mi...	12324226	21303	39	1411271
Caelo	Prednisolone, mi...	13343105	21449	60	1411232
Caelo	Prednisolone, mi...	154000	22435	60	20160225*
Caelo	Prednisolone, mi...	154000	22435SI	59	20160225*
Caelo	Prednisolone, mi...	161343	22467	60	20160601*
Caelo	Prednisolone, mi...	161343	22467SI	44	20160601*
Caelo	Prednisolone, mi...	15400002	22783	40	20160225
Caelo	Prednisolone, mi...	15400002	22783SI	40	20160225
Euro OTC	Prednisolone, mi...	1212021-02	21604	60	1411270
Euro OTC	Prednisolone, mi...	1212021-02	21604SI	48	1411270
Euro OTC	Prednisolone, mi...	1501047-01	21849	60	AR-15-FG-015509-01
Euro OTC	Prednisolone, mi...	1501047-01	21849SI	30	AR-15-FG-015509-01
Euro OTC	Prednisolone, mi...	1607011	22709	40	20160818*
Euro OTC	Prednisolone, mi...	1607011	22709SI	40	20160818*
Fagron	Prednisolone, mi...	13H07-B02-285592	21660	60	20130909
Fagron	Prednisolone, mi...	13H07-B02-285592	21660SI	60	20130909
Fagron	Prednisolone, mi...	14I10-B03-302263	22651	40	20141020
Fagron	Prednisolone, mi...	14I10-B03-302263	22651SI	40	20141020
Fagron	Prednisolone, mi...	16C15-B01-320761	22803	40	20160407
Fagron	Prednisolone, mi...	16C15-B01-320761	22803SI	36	20160407

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 996 spectra of 21 reference samples from the substance/substance group *Prednisolone, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 12 different batches.
- 109 693 spectra from a total of 1954 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 382 spectra of 11 reference samples from the substance/substance group *Prednisolone, micronized*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prednisolone, micronized	172777	23846	40
Euro OTC	Prednisolone, micronized	1702020	23180	40
Euro OTC	Prednisolone, micronized	1905005	24602	40
Fagron	Prednisolone, micronized	1108055-04	20855	40
Fagron	Prednisolone, micronized	16E09-B07-328220	23260	40
Caelo	Prednisolone, micronized	13343105	21451SI	60
Caelo	Prednisolone, micronized	161343	22467SI [†]	3
Caelo	Prednisolone, micronized	172777	23846SI	38
Euro OTC	Prednisolone, micronized	1702020	23180SI	21
Euro OTC	Prednisolone, micronized	1905005	24602SI	40
Fagron	Prednisolone, micronized	16E09-B07-328220	23260SI	20

- 118 760 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1352 spectra from 444 *Apo-Ident* customers from 297 batches from the substance/substance group *Prednisolone, micronized*.
- Among them are spectra of independent samples from 275 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H. 05.03.13 ek: 14,08EUR	Prednisolone, micronized	12D30-N04	1
AHD	Prednisolone, micronized	121202103	1
AHD	Prednisolone, micronized	1212021-03	1
AHD	Prednisolone, micronized	160711-01	1
AHD	Prednisolone, micronized	1702020-01	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Prednisolone, micronized	13343106	1
Euro OTC	Prednisolone, micronized	12021-03	1
Fagron	Prednisolone, micronized	14A30-B02-294968	4
anzag	Prednisolone, micronized	14B18-B05-294966	1
Apomix	Prednisolone, micronized	16H04-B03-332930	1
Apotheke Mildenau	Prednisolone, micronized	1108055-04	3
Berkel AHK	Prednisolone, micronized	13343115	1
Bomastus / Alliance Hea...	Prednisolone, micronized	16134305	1
Bombastus	Prednisolone, micronized	17F07-B05-341578	2
Bombastus	Prednisolone, micronized	17F07-B05-341574	2
Caelo	Prednisolone, micronized	16134301	8
Caelo	Prednisolone, micronized	702020-01	1
Caelo	Prednisolone, micronized	11/26-N04	1
Caelo	Prednisolone, micronized	10196625	1
Caelo	Prednisolone, micronized	20021303	1
Caelo	Prednisolone, micronized	12324205	12
Caelo	Prednisolone, micronized	1234205	1
Caelo	Prednisolone, micronized	2413Q02105	1
Caelo	Prednisolone, micronized	12324217	5
Caelo	Prednisolone, micronized	10196604	1
Caelo	Prednisolone, micronized	4513U2105	1
Caelo	Prednisolone, micronized	1511011	1
Caelo	Prednisolone, micronized	12324203	3
Caelo	Prednisolone, micronized	12324219	7
Caelo	Prednisolone, micronized	411092-1-P	1
Caelo	Prednisolone, micronized	9193501	1
Caelo	Prednisolone, micronized	13343113	1
Caelo	Prednisolone, micronized	13343116	4
Caelo	Prednisolone, micronized	15055102	6
Caelo	Prednisolone, micronized	13343104	10
Caelo	Prednisolone, micronized	13343114	5
Caelo	Prednisolone, micronized	13343112	1
Caelo	Prednisolone, micronized	19081504	1
Caelo	Prednisolone, micronized	15206108	13
Caelo	Prednisolone, micronized	15206105	7
Caelo	Prednisolone, micronized	1212021-03	6
Caelo	Prednisolone, micronized	15400003	24
Caelo	Prednisolone, micronized	1501047-02	3
Caelo	Prednisolone, micronized	16A20-B03-316421	1
Caelo	Prednisolone, micronized	60367086	2
Caelo	Prednisolone, micronized	16134305	14
Caelo	Prednisolone, micronized	16E09-B07-328150	3
Caelo	Prednisolone, micronized	161343032	1
Caelo	Prednisolone, micronized	1613414	1
Caelo	Prednisolone, micronized	16134314	18
Caelo	Prednisolone, micronized	17f07-b05	1
Caelo	Prednisolone, micronized	1702020-02	2
Caelo	Prednisolone, micronized	17277702	4
Caelo	Prednisolone, micronized	17277706	4
Caelo	Prednisolone, micronized	1727704	1
Caelo	Prednisolone, micronized	17277716	8
Caelo	Prednisolone, micronized	1727716	1
Caelo	Prednisolone, micronized	17277720	2
Caelo	Prednisolone, micronized	10196627	7
Caelo	Prednisolone, micronized	15K03-B04-314358	1
Caelo	Prednisolone, micronized	16034301	2
Caelo	Prednisolone, micronized	13343111	4
Caelo	Prednisolone, micronized	10196611	3
Caelo	Prednisolone, micronized	12171303	2
Caelo	Prednisolone, micronized	12324220	2

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Supplier	Substance	Batch	Spectra
Caelo	Prednisolone, micronized	16C15-B01_320761	1
Caelo	Prednisolone, micronized	NEPL180603	1
Caelo	Prednisolone, micronized	15206102	18
Caelo	Prednisolone, micronized	1234556	1
Caelo	Prednisolone, micronized	10196622	2
Caelo	Prednisolone, micronized	1607011-01	3
Caelo	Prednisolone, micronized	17F07-B05-341574	1
Caelo	Prednisolone, micronized	13E15-N06	4
Caelo	Prednisolone, micronized	13343115	9
Caelo	Prednisolone, micronized	14B18-B05-294966	2
Caelo	Prednisolone, micronized	13A07-N14	1
Caelo	Prednisolone, micronized	14/10-B03-302266	1
Caelo	Prednisolone, micronized	15400010	5
Caelo	Prednisolone, micronized	16134314/2120418	1
Caelo	Prednisolone, micronized	3344	1
Caelo	Prednisolone, micronized	12324216	9
Caelo	Prednisolone, micronized	16134302	13
Caelo	Prednisolone, micronized	152006105	1
Caelo	Prednisolone, micronized	4712I-02105	1
Caelo	Prednisolone, micronized	133414	1
Caelo	Prednisolone, micronized	121202102	1
Caelo	Prednisolone, micronized	16C15-B01-324942	1
Caelo	Prednisolone, micronized	12324207	4
Caelo	Prednisolone, micronized	12324204	4
Caelo	Prednisolone, micronized	12324221	2
Caelo	Prednisolone, micronized	1212021-01	1
Caelo	Prednisolone, micronized	1250216	1
Caelo	Prednisolone, micronized	15400001	2
Caelo	Prednisolone, micronized	16134306	4
Caelo	Prednisolone, micronized	17020-01	1
Caelo	Prednisolone, micronized	17277703	9
Caelo	Prednisolone, micronized	16134310	24
Caelo	Prednisolone, micronized	16C15-B01-320761	1
Caelo	Prednisolone, micronized	NEPL160202	1
Caelo	Prednisolone, micronized	12185702	2
Caelo	Prednisolone, micronized	16134303	1
Caelo	Prednisolone, micronized	13343106	7
Caelo	Prednisolone, micronized	15055101	6
Caelo	Prednisolone, micronized	15206103	9
Caelo	Prednisolone, micronized	15400004	19
Caelo	Prednisolone, micronized	16C15-B01-321979	2
Caelo	Prednisolone, micronized	16134316	15
Caelo	Prednisolone, micronized	1702020-01	1
Caelo	Prednisolone, micronized	13343107	1
Caelo	Prednisolone, micronized	14/10B03302265	1
Caelo	Prednisolone, micronized	16134315	13
Caelo	Prednisolone, micronized	17277710	2
Caelo	Prednisolone, micronized	17277723	1
Caelo	Prednisolone, micronized	10196606	1
Caelo	Prednisolone, micronized	1501047-01	3
Caelo	Prednisolone, micronized	1540003	1
Caelo	Prednisolone, micronized	17277711	7
Caelo	Prednisolone, micronized	1727710	1
Caelo	Prednisolone, micronized	10196626	6
Caelo	Prednisolone, micronized	12171302	1
Caelo	Prednisolone, micronized	12324213	7
Caelo	Prednisolone, micronized	1232417	1
Caelo	Prednisolone, micronized	13343101	1
Caelo	Prednisolone, micronized	14G30-B14-302262	1
Caelo	Prednisolone, micronized	15206106	1

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Supplier	Substance	Batch	Spectra
Caelo	Prednisolone, micronized	16E09-B07-328220	1
Caelo	Prednisolone, micronized	18138113	1
Caelo	Prednisolone, micronized	17F07-B05-341578	1
Caelo	Prednisolone, micronized	k04c20121219	1
Caesar & Loretz GmbH	Prednisolone, micronized	12324205	1
Caesar & Loretz GmbH	Prednisolone, micronized	12324219	1
Caesar & Loretz GmbH	Prednisolone, micronized	15206101	2
Caesar & Loretz GmbH	Prednisolone, micronized	17277702	2
Caesar & Loretz GmbH	Prednisolone, micronized	17277704	1
Caesar & Loretz GmbH	Prednisolone, micronized	17277711	3
Caesar & Loretz GmbH	Prednisolone, micronized	17277716	3
Caesar & Loretz GmbH	Prednisolone, micronized	17277723	1
Caesar & Loretz GmbH/Go...	Prednisolone, micronized	17277711	1
Caesar & Loretz GmbH/Mi...	Prednisolone, micronized	17277711	1
Caesar u. Loretz/Noweda	Prednisolone, micronized	16134301	1
Caesar&Loretz GmbH/Anzag	Prednisolone, micronized	13343112	1
Caesar/Lorenz	Prednisolone, micronized	12324204	1
Caolo- Noweda	Prednisolone, micronized	15206103	1
Cealo/Noweda	Prednisolone, micronized	1526108	1
EuRho	Prednisolone, micronized	1012012-02	2
EuRho	Prednisolone, micronized	1012012-01	1
EuRho	Prednisolone, micronized	1108055-03	2
EuRho	Prednisolone, micronized	1702020-02	1
EuRho/Jenne	Prednisolone, micronized	1108055-04	2
EuRho/Noweda	Prednisolone, micronized	1702020-01	1
Euro OTC	Prednisolone, micronized	1108055-04	15
Euro OTC	Prednisolone, micronized	110805504	4
Euro OTC	Prednisolone, micronized	1108055-01	1
Euro OTC	Prednisolone, micronized	NEPL110103	1
Euro OTC	Prednisolone, micronized	121202101	1
Euro OTC	Prednisolone, micronized	16E09-B07-329686	2
Euro OTC	Prednisolone, micronized	14/10-B03-302263	1
Euro OTC	Prednisolone, micronized	15400010	1
Euro OTC	Prednisolone, micronized	1702020-01	38
Euro OTC	Prednisolone, micronized	170202201	1
Euro OTC	Prednisolone, micronized	1501047-03	4
Euro OTC	Prednisolone, micronized	18A29-B02-348044	1
Euro OTC	Prednisolone, micronized	150104743	1
Euro OTC	Prednisolone, micronized	30042014B	1
Euro OTC	Prednisolone, micronized	150104701	3
Euro OTC	Prednisolone, micronized	170202001	2
Euro OTC	Prednisolone, micronized	1702020-02	24
Euro OTC	Prednisolone, micronized	1108055-02	2
Euro OTC	Prednisolone, micronized	190500501	2
Euro OTC	Prednisolone, micronized	1212021-01	26
Euro OTC	Prednisolone, micronized	1501047	1
Euro OTC	Prednisolone, micronized	1501047-02	15
Euro OTC	Prednisolone, micronized	13343104	1
Euro OTC	Prednisolone, micronized	1314Q2105	1
Euro OTC	Prednisolone, micronized	1212021-03	38
Euro OTC	Prednisolone, micronized	501047-01	1
Euro OTC	Prednisolone, micronized	1702020-03	13
Euro OTC	Prednisolone, micronized	170202002	3
Euro OTC	Prednisolone, micronized	1702020-03	1
Euro OTC	Prednisolone, micronized	170202-03	1
Euro OTC	Prednisolone, micronized	1905005-01	12
Euro OTC	Prednisolone, micronized	15010477-01	1
Euro OTC	Prednisolone, micronized	150104747-01	1
Euro OTC	Prednisolone, micronized	1012012-02	2
Euro OTC	Prednisolone, micronized	118055-04	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Euro/ Sanacorp	Prednisolone, micronized	121202103	1
Euro/Phoenix	Prednisolone, micronized	190500501	1
Euro/Phoenix	Prednisolone, micronized	190500502	1
euroct/gehe	Prednisolone, micronized	1212021-01	1
euroct/Gehe	Prednisolone, micronized	1212021-01	1
Euro OTC	Prednisolone, micronized	1607011-01	30
Euro OTC	Prednisolone, micronized	121021-01	2
Euro OTC	Prednisolone, micronized	1108055-03	10
Euro OTC	Prednisolone, micronized	16134308	3
Euro OTC	Prednisolone, micronized	121202102	2
Euro OTC	Prednisolone, micronized	1212021	1
Europharm/Otto	Prednisolone, micronized	1108055-03	1
Europharm/Otto	Prednisolone, micronized	1108055-04	5
europharma	Prednisolone, micronized	1002001240	1
Fagron	Prednisolone, micronized	130F-N04	1
Fagron	Prednisolone, micronized	16C15B01320761	1
Fagron	Prednisolone, micronized	12C22-N05	7
Fagron	Prednisolone, micronized	12D30-N04	1
Fagron	Prednisolone, micronized	11G22-N08	1
Fagron	Prednisolone, micronized	4313E-02105	1
Fagron	Prednisolone, micronized	K04C20121006	1
Fagron	Prednisolone, micronized	13DE15-N06	1
Fagron	Prednisolone, micronized	13H07-B02-285593	3
Fagron	Prednisolone, micronized	13H07-B02-285590	3
Fagron	Prednisolone, micronized	13A07N14	1
Fagron	Prednisolone, micronized	13H07-B02	2
Fagron	Prednisolone, micronized	K04C20131102	1
Fagron	Prednisolone, micronized	1410-B03	1
Fagron	Prednisolone, micronized	14/10-B03-302265	3
Fagron	Prednisolone, micronized	14B18-B05294966	1
Fagron	Prednisolone, micronized	14/10B03302265	1
Fagron	Prednisolone, micronized	K04C20140502	2
Fagron	Prednisolone, micronized	14G30-B14	1
Fagron	Prednisolone, micronized	14i10-b03-302269	1
Fagron	Prednisolone, micronized	15D14-B01-308425	3
Fagron	Prednisolone, micronized	14/10-B03-302271	1
Fagron	Prednisolone, micronized	15k03-b04-314226	1
Fagron	Prednisolone, micronized	15B18-B05-294969	1
Fagron	Prednisolone, micronized	16A20-B03-319015	7
Fagron	Prednisolone, micronized	15K03-B04-314869	1
Fagron	Prednisolone, micronized	16A20-B03	4
Fagron	Prednisolone, micronized	15K03B04314226	1
Fagron	Prednisolone, micronized	2834	1
Fagron	Prednisolone, micronized	16A20-B03-316421	1
Fagron	Prednisolone, micronized	15K03-B04-314357	2
Fagron	Prednisolone, micronized	150528P	1
Fagron	Prednisolone, micronized	16C15-B01-321979	15
Fagron	Prednisolone, micronized	15K03-B04	1
Fagron	Prednisolone, micronized	16C15-B01	1
Fagron	Prednisolone, micronized	1717M-02105	1
Fagron	Prednisolone, micronized	16c15-b02	1
Fagron	Prednisolone, micronized	16c15-802	1
Fagron	Prednisolone, micronized	16C15-B02-324945	1
Fagron	Prednisolone, micronized	16E09/B07/328220	1
Fagron	Prednisolone, micronized	16E09-B07_328220	1
Fagron	Prednisolone, micronized	16E09-B07-328220	6
Fagron	Prednisolone, micronized	16E09-B07-329686	1
Fagron	Prednisolone, micronized	16E09-B075411	1
Fagron	Prednisolone, micronized	1711021A	1
Fagron	Prednisolone, micronized	16H04-B03-332930	7

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Prednisolone, micronized	NEPL160202	1
Fagron	Prednisolone, micronized	17F07-B05-341575	3
Fagron	Prednisolone, micronized	17F07-B05	3
Fagron	Prednisolone, micronized	16e09-B07-329686	1
Fagron	Prednisolone, micronized	NEPL160705	1
Fagron	Prednisolone, micronized	NEPL170210	1
Fagron	Prednisolone, micronized	NEPL170605	2
Fagron	Prednisolone, micronized	18A29-B02-348044	1
Fagron	Prednisolone, micronized	18H07-804	1
Fagron	Prednisolone, micronized	18h07-b04-353326	1
Fagron	Prednisolone, micronized	18H07-B04-355631	2
Fagron	Prednisolone, micronized	18H07-B04-353326	2
Fagron	Prednisolone, micronized	17014-801-340448	1
Fagron	Prednisolone, micronized	16C15-B01-321979	1
Fagron	Prednisolone, micronized	17D14-B01	1
Fagron	Prednisolone, micronized	13E15-N06	16
Fagron	Prednisolone, micronized	16H04-B03-332929	12
Fagron	Prednisolone, micronized	19E28-B13-191224	1
Fagron	Prednisolone, micronized	18A29-B02	1
Fagron	Prednisolone, micronized	18C19-B07	1
Fagron	Prednisolone, micronized	11D13-N05	1
Fagron	Prednisolone, micronized	12K14-N03	10
Fagron	Prednisolone, micronized	14B18-B05-294969	2
Fagron	Prednisolone, micronized	18C19-B07-353242	3
Fagron	Prednisolone, micronized	12c22-N05	1
Fagron	Prednisolone, micronized	18A29-B02-348540	2
Fagron	Prednisolone, micronized	1410-B03-302269	2
Fagron	Prednisolone, micronized	18C19-B07-351226	2
Fagron	Prednisolone, micronized	12324216	1
Fagron	Prednisolone, micronized	K04C20121006	1
Fagron	Prednisolone, micronized	K04C20130203M	1
Fagron	Prednisolone, micronized	14818-B05-294966	1
Fagron	Prednisolone, micronized	13E15-N06	1
Fagron	Prednisolone, micronized	12D30-N04	9
Fagron	Prednisolone, micronized	13A07-N14	6
Fagron	Prednisolone, micronized	13E13-N06	1
Fagron	Prednisolone, micronized	613Q-02105	1
Fagron	Prednisolone, micronized	13J28-B06	2
Fagron	Prednisolone, micronized	14L10-B03-302269	1
Fagron	Prednisolone, micronized	16C15-B02-324943	5
Fagron	Prednisolone, micronized	17D14-B01-338573	4
Fagron	Prednisolone, micronized	17F07-B05-341574	4
Fagron	Prednisolone, micronized	17G28-B03-345538	5
Fagron	Prednisolone, micronized	NEPL151202	1
Fagron	Prednisolone, micronized	14I10-B03-302269	2
Fagron	Prednisolone, micronized	11J26-N04	2
Fagron	Prednisolone, micronized	17G28-B03-345539	3
Fagron	Prednisolone, micronized	13H07-B020	1
Fagron	Prednisolone, micronized	NEPL170209	2
Fagron	Prednisolone, micronized	1607011-01	2
Fagron	Prednisolone, micronized	18H07-B04-355630	1
Fagron	Prednisolone, micronized	NPL190306	1
Fagron	Prednisolone, micronized	13J28-B06-289670	3
Fagron	Prednisolone, micronized	13H7-B02-285590	1
Fagron	Prednisolone, micronized	14B18-B05	1
Fagron	Prednisolone, micronized	14/10-B03-302266	2
Fagron	Prednisolone, micronized	14I10-B03-302266	1
Fagron	Prednisolone, micronized	15K03-B04-314358	6
Fagron	Prednisolone, micronized	15K03_B04_314226	1
Fagron	Prednisolone, micronized	16C15-B02	1

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Supplier	Substance	Batch	Spectra
Fagron	Prednisolone, micronized	14/10-B03	1
Fagron	Prednisolone, micronized	17G2B03-345538	1
Fagron	Prednisolone, micronized	18H07-B04	2
Fagron	Prednisolone, micronized	13H07-B02-285593	1
Fagron	Prednisolone, micronized	14G30-B14-302262	4
Fagron	Prednisolone, micronized	14I10-B03	1
Fagron	Prednisolone, micronized	14/10-B03-302269	1
Fagron	Prednisolone, micronized	1501047-02	1
Fagron	Prednisolone, micronized	16C15-B01-324942	5
Fagron	Prednisolone, micronized	17g2828-b03-345539	1
Fagron	Prednisolone, micronized	18C19-B07-351225	1
Fagron	Prednisolone, micronized	14B18-B05-294966	10
Fagron	Prednisolone, micronized	1212021-02	2
Fagron	Prednisolone, micronized	14I10-B03-302265	2
Fagron	Prednisolone, micronized	15D14-B01	1
Fagron	Prednisolone, micronized	15K03-B04-314226	12
Fagron	Prednisolone, micronized	16A20-B03-316420	7
Fagron	Prednisolone, micronized	16C15-B01-319992	2
Fagron	Prednisolone, micronized	16E09-B07-328150	11
Fargo	Prednisolone, micronized	12D30-N04	1
Fargon	Prednisolone, micronized	FP01409P	1
Fargon	Prednisolone, micronized	16134308	1
Fargon/AHD	Prednisolone, micronized	18A29-B02-348044	1
Euro OTC	Prednisolone, micronized	121221-03	1
Fischar/Gehe	Prednisolone, micronized	14A30-B02-294968	1
Fragon	Prednisolone, micronized	18C19-B07-351225	1
Fragon/Phoenix	Prednisolone, micronized	15K03-B04-314226	1
Fragon/Phoenix	Prednisolone, micronized	16C15-B02-324943	1
Gehe	Prednisolone, micronized	12C22-N05	1
Gehe	Prednisolone, micronized	13A07-N14	2
Gehe	Prednisolone, micronized	12324216	2
Gehe	Prednisolone, micronized	13E15-No6	1
Gehe	Prednisolone, micronized	1212021-01	4
Gehe	Prednisolone, micronized	13343107	1
Gehe	Prednisolone, micronized	14A30-B02-294968	1
Gehe	Prednisolone, micronized	1212021-02	1
Gehe	Prednisolone, micronized	1501047-01	2
Gehe	Prednisolone, micronized	16C15-B01	1
Gehe	Prednisolone, micronized	16C-15-B02	1
Gehe	Prednisolone, micronized	16134302	1
Gehe	Prednisolone, micronized	16E09-B07	1
Gehe	Prednisolone, micronized	16134314	1
Gehe	Prednisolone, micronized	17F07-B05-341574	1
Gehe	Prednisolone, micronized	17G28-B03	1
Gehe	Prednisolone, micronized	18H07-B04	1
Gehe	Prednisolone, micronized	18H07-B04-355631	1
Gehe	Prednisolone, micronized	19H19-B02	1
GEHE	Prednisolone, micronized	1702020-02	1
Caelo	Prednisolone, micronized	14A30-B02-294968	1
Bombastus	Prednisolone, micronized	1501047-02	1
Caelo	Prednisolone, micronized	150104701	2
Fagron	Prednisolone, micronized	15K03-B04-314226	1
Fagron	Prednisolone, micronized	16C15B01321979	1
Fagron	Prednisolone, micronized	17F07-B05-341578	1
Fagron	Prednisolone, micronized	16c15-B01-320761	1
Gehe/Fragon	Prednisolone, micronized	16E09B07328150	1
Caelo	Prednisolone, micronized	1410B03302265	1
Fagron	Prednisolone, micronized	14110-B03302265	1
Gehe-Fragon	Prednisolone, micronized	14B18B05294966	1
Hedinger	Prednisolone, micronized	P2018/116	1

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Supplier	Substance	Batch	Spectra
Henan Lihua/Gehe	Prednisolone, micronized	1501047-01	1
Ichthyol / Phoenix	Prednisolone, micronized	16C15-B01-320761	1
Ichthyol gesellschaft	Prednisolone, micronized	15400003	1
Caelo	Prednisolone, micronized	17277704	20
Fagron	Prednisolone, micronized	18H07-B04-354523	5
Krieger	Prednisolone, micronized	3416	1
Noweda	Prednisolone, micronized	10196626	2
Noweda	Prednisolone, micronized	1212021-02	1
Noweda	Prednisolone, micronized	1108055-05	1
Noweda	Prednisolone, micronized	15206101	1
Noweda	Prednisolone, micronized	1607011-01	1
Caelo	Prednisolone, micronized	16134308	6
Fagron	Prednisolone, micronized	17D14-Bo1-338573	1
Fagron	Prednisolone, micronized	17G28-B03	1
Phoenix	Prednisolone, micronized	11j26-N04	2
Phoenix	Prednisolone, micronized	15400003	1
Phoenix	Prednisolone, micronized	16134310	1
Phoenix	Prednisolone, micronized	16134315	1
Phoenix	Prednisolone, micronized	3220	1
Phoenix	Prednisolone, micronized	17277703	1
Phoenix	Prednisolone, micronized	17277711	1
phoenix 5.4.2013	Prednisolone, micronized	1108055-04	1
Caelo	Prednisolone, micronized	1905005-01	1
phönix	Prednisolone, micronized	17277716	1
Phönix	Prednisolone, micronized	13E15-N06	2
Phönix	Prednisolone, micronized	13A07N14	1
Phönix	Prednisolone, micronized	12324216	1
Phönix	Prednisolone, micronized	14B18-B05-294966	1
Phönix	Prednisolone, micronized	17277723	1
Phönix Gotha	Prednisolone, micronized	12324213	1
Phönix Gotha	Prednisolone, micronized	12324217	1
Phönix Gotha	Prednisolone, micronized	1232417	1
Phönix Gotha	Prednisolone, micronized	13343105	1
Phönix Gotha	Prednisolone, micronized	13343112	2
Phönix Gotha	Prednisolone, micronized	13343111	1
Caelo	Prednisolone, micronized	12171306	2
Caelo	Prednisolone, micronized	15206101	8
Phönix/Euro	Prednisolone, micronized	1702020-02	1
Phönix/Euro	Prednisolone, micronized	1501047-03	1
Fagron	Prednisolone, micronized	14B18-Bo5-294966	1
sanacorp	Prednisolone, micronized	14/10-B03-302266	1
Sanacorp	Prednisolone, micronized	1108055-03	1
Sanacorp	Prednisolone, micronized	13E15-N06	1
Sanacorp	Prednisolone, micronized	12324221	1
Sanacorp	Prednisolone, micronized	13j28-b06-289670	1
Sanacorp	Prednisolone, micronized	14/10-B03-302269	1
Sanacorp	Prednisolone, micronized	16H04-B03_332930	1
Sanacorp	Prednisolone, micronized	18AB02	1
Sanacorp WE:01.08.2016 ...	Prednisolone, micronized	1501047-01	1
Caelo	Prednisolone, micronized	12171301	6
Sonnenberg-Apotheke	Prednisolone, micronized	12324219	1
Tianyao Pharma/Phönix	Prednisolone, micronized	NEPL110103	1
Tianyao Pharma/Phönix	Prednisolone, micronized	1212021-01	1
Euro OTC	Prednisolone, micronized	1501047-01	26
Caelo	Prednisolone, micronized	12324226	6
Euro OTC	Prednisolone, micronized	1212021-02	26
Caelo	Prednisolone, micronized	12324202	11
Caelo	Prednisolone, micronized		2
Caelo	Prednisolone, micronized	13343105	4
Caelo	Prednisolone, micronized	15400002	17

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Supplier	Substance	Batch	Spectra
Fagron	Prednisolone, micronized	13H07-B02-285592	4
Fagron	Prednisolone, micronized	16C15-B01-320761	3
Fagron	Prednisolone, micronized		1

- 109 895 spectra from 742 *Apo-Ident* customers from a total of 31 597 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednisolone, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednisolone, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	996	0	109 693
Type B	0	382	0	118 760
Type C	0	1332	20	109 895

The substance/substance group *Prednisolone, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.3976 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.4293 %)
Type C	100.0000 % (> 99.8899 %)	98.5207 % (> 98.2988 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednisolone, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisolon dihydrogen phosphate dinat...	17.07	–
Betamethasone, micronized	23.16	159.70
Dexamethasone	24.17	58.39
Triamcinolone acetonide	24.79	60.79

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Substanz	Distance in main model	Distance in second-stage model
Cyanocobalamin	26.55	—
Methylprednisolone	35.77	—
Hydrocortisone acetate	42.42	—
Naloxone hydrochloride dihydrate	47.05	—
Sodium edetate	49.25	—
Fluocinolonacetamid, micronized	52.14	—
⋮	⋮	⋮
Budesonide, micronized	>50	60.99
Prednicarbate, micronized	>50	75.69
Triamcinolone, micronized	>50	80.72
Betamethasone valerate	>50	81.30
Prednisone	>50	112.53
Erythromycin	>50	131.14
Capsaicin	>50	189.79
Heparin sodium	>50	201.44
Norethisterone acetate	>50	260.06

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednisolone, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21449	21449	0.00	38.82
22467	22467	0.00	20.27
22783	22435	2.26	17.07
21303	21303	0.00	38.32
21604	21604	0.00	17.97
22435	22435	0.00	18.62
21660	21449	1.42	39.42
22803	22435	3.63	18.18
22651	21303	5.45	40.28
21849	21849	0.00	22.11
20773	21303	6.40	41.62
22709	22709	0.00	19.18

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prednisone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20002-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prednisone; Prednisonum

Special notes

When selecting the *Prednisone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prednisone	6	3	40

Second-stage model

For differentiation of the substance/substance group *Prednisone* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prednisone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prednisone	12232716	21408	60	20120829
Caelo	Prednisone	12232716	21409	60	20120829
Caelo	Prednisone	192455	24895	40	31102019*
Euro OTC	Prednisone	1401042-02	21616	60	1605276
Euro OTC	Prednisone	1604051	22557	40	20160523*
Euro OTC	Prednisone	1604051	22557SI	40	20160523*
Fagron	Prednisone	13C14-B40-289148	21573	60	20131223
Fagron	Prednisone	16J19-B02-328642	23227	40	20161221

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 8 reference samples from the substance/substance group *Prednisone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 289 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 369 spectra of 10 reference samples from the substance/substance group *Prednisone*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prednisone	171665	23341	20
Caelo	Prednisone	17166504	23578	30
Euro OTC	Prednisone	1702008	23179	40
Caelo	Prednisone	12232716	21408SI [†]	60
Caelo	Prednisone	12232716	21409SI [†]	60
Caelo	Prednisone	171665	23341SI	30
Caelo	Prednisone	17166504	23578SI	30
Caelo	Prednisone	192455	24895SI [†]	40
Euro OTC	Prednisone	1702008	23179SI	29
Fagron	Prednisone	16J19-B02-328642	23227SI [†]	30

- 118 773 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 69 spectra from 38 *Apo-Ident* customers from 41 batches from the substance/substance group *Prednisone*.
- Among them are spectra of independent samples from 40 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Prednisone	204312107	1
Caelo	Prednisone	10037817	1
Caelo	Prednisone	28021401	1
Caelo	Prednisone	28021403	1
Caelo	Prednisone	12232712	1
Caelo	Prednisone	12232714	1
Caelo	Prednisone	13262302	1
Caelo	Prednisone	15218606	5
Caelo	Prednisone	13262304	3
Caelo	Prednisone	15218607	1
Caelo	Prednisone	16277206	1
Caelo	Prednisone	16277201	1
Caelo	Prednisone	17166502	2
Caelo	Prednisone	17166507	3
Caelo	Prednisone	17166504	1
Caelo	Prednisone	12232713	1
Caelo	Prednisone	17166501	2
Caelo	Prednisone	2114Q2107	1
Caelo	Prednisone	15218602	4

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Prednisone	5087	1
Caelo	Prednisone	17166503	1
Caelo	Prednisone	12232705	3
Caelo	Prednisone	10037826	1
Euro OTC	Prednisone	150043-03	1
Euro OTC	Prednisone	1501043-02	1
Euro OTC	Prednisone	1702008-01	2
Euro OTC	Prednisone	1501043-01	2
Euro OTC	Prednisone	1501043-03	5
Euro OTC	Prednisone	1604051-01	3
Fagron	Prednisone	21021401	1
Fagron	Prednisone	16H04-B04-334368	1
Fagron	Prednisone	12E02-N10	1
Fagron	Prednisone	12E02-N01	1
Fagron	Prednisone	13C13-N08	1
Fagron	Prednisone	15218608	1
Gehe	Prednisone	12L14-M03	1
Gehe	Prednisone	13C13-N08	1
Gehe	Prednisone	12232714	1
Gehe	Prednisone	17166508	1
Caelo	Prednisone	12177604	1
Noweda	Prednisone	17166501	1
Phönix	Prednisone	11D08-N05	1
Euro OTC	Prednisone	1604501-01	1
sanacorp	Prednisone	13262302	1
Sanacorp	Prednisone	16277206	1
Euro OTC	Prednisone	1401042-02	1

- 111 178 spectra from 742 *Apo-Ident* customers from a total of 31 850 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prednisone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prednisone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	369	0	118 773
Type C	0	68	1	111 178

The substance/substance group *Prednisone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3740 %)
Type C	100.0000 % (> 99.8899 %)	98.5507 % (> 94.2029 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prednisone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Gramicidin	19.48	—
Triamcinolone, micronized	22.10	196.80
Polymyxin B sulfate	24.37	—
Magnesium citrate	31.16	—
Bacitracin	34.16	—
Prednisolone acetate	38.99	—
Cyanocobalamin	39.14	—
Tyrothricin	43.72	—
Minoxidil	49.25	—
⋮	⋮	⋮
Capsaicin	>50	56.93
Triamcinolone acetonide	>50	122.78
Dexamethasone	>50	123.48
Betamethasone valerate	>50	138.59
Betamethasone, micronized	>50	159.34
Prednisolone, micronized	>50	161.99
Erythromycin	>50	166.08
Budesonide, micronized	>50	173.45
Prednicarbate, micronized	>50	232.86
Norethisterone acetate	>50	251.11
Heparin sodium	>50	307.75

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prednisone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22557	22557	0.00	24.93
21616	21616	0.00	22.10

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21573	21616	5.34	25.86
23227	24895	2.79	26.29
21408	24895	5.81	27.80
21409	21616	5.04	25.86
24895	24895	0.00	26.39

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Pregnenolone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20721-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pregnenolone; Pregnenolonum

Special notes

When selecting the *Pregnenolone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pregnenolone	8	4	19

Second-stage model

For differentiation of the substance/substance group *Pregnenolone* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pregnenolone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Pregnenolone	1204040-01	20721	40	1404311
Euro OTC	Pregnenolone	1312007-01	21679	60	8985
Euro OTC	Pregnenolone	1602001	22375	45	20160208*
Euro OTC	Pregnenolone	1612019	22979	40	20170131*
Euro OTC	Pregnenolone	1908021	24849	40	20190913*
Euro OTC	Pregnenolone	1908020	24932	40	20191018*
Fagron	Pregnenolone	15B11-B07-310278	22355	45	9338
Fagron	Pregnenolone	18L27-B02-357840	24704	40	20190220

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 350 spectra of 8 reference samples from the substance/substance group *Pregnenolone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 339 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Pregnenolone*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Pregnenolone	1606028	22706	40
Euro OTC	Pregnenolone	1709017	23696	40
Euro OTC	Pregnenolone	1909013	24954	40
Euro OTC	Pregnenolone	2001037	25129	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 85 spectra from 12 *Apo-Ident* customers from 20 batches from the substance/substance group *Pregnenolone*.
- Among them are spectra of independent samples from 19 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Pregnenolone	APC07-150801(M)P	3
Audor Pharma	Pregnenolone	AP1109007-01P	1
Audor Pharma	Pregnenolone	AP10L10-M01P	1
Audor Pharma	Pregnenolone	APC07-160801(M)P	2
Audor Pharma	Pregnenolone	APC07-180201	2
Audor Pharma	Pregnenolone	APC07-180201(M)P	3
Euro OTC	Pregnenolone	1606028-01	10
Euro OTC	Pregnenolone	1602001-01	1
Euro OTC	Pregnenolone	1612019-01	51
Fagron	Pregnenolone	14B18-B04-291917	1
Fagron	Pregnenolone	16L29-B02331611	1
gehe	Pregnenolone	Apc07160801	1
Haihang Industry	Pregnenolone	20140329	1
Koisser	Pregnenolone	ZH-130802	1
Koisser Pharma	Pregnenolone	ZH-131001	1
KS Pharma	Pregnenolone	ZH-111119	1
NWM CHina	Pregnenolone	PR150329	1
NWM Shandong Northwest ...	Pregnenolone	PRN151219	1
Euro OTC	Pregnenolone	1402025-01	1
Euro OTC	Pregnenolone	1312007-01	1

- 111 162 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pregnenolone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pregnenolone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	350	0	110 339
Type B	0	160	0	118 982
Type C	0	85	0	111 162

The substance/substance group *Pregnenolone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2857 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 92.9412 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pregnenolone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Norethisterone acetate	24.89	—
Budesonide, micronized	36.66	—
Progesterone, micronized	37.97	156.74
Testosterone propionate	43.04	259.20
Prasterone	43.89	—
Wool alcohols	43.97	—
Cholesterol	44.18	—
Testosterone	44.20	—
Estradiol valerate	52.84	—
⋮	⋮	⋮
Estriol	>50	82.32
Spirolactone	>50	212.42
Alfatradiol	>50	298.74
Quinine hydrochloride	>50	337.33
Quinine sulfate	>50	543.46

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Pregnenolone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20721	20721	0.00	27.22
21679	21679	0.00	24.89
22979	22979	0.00	28.54
24932	24932	0.00	31.60
22375	22375	0.00	27.39
24849	24849	0.00	28.08
22355	22355	0.00	33.09
24704	22375	6.43	33.02

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Prilocaine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21048-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Prilocaine hydrochloride; Prilocaini hydrochloridum

Special notes

When selecting the *Prilocaine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Prilocaine hydrochloride	3	1	13

Second-stage model

For differentiation of the substance/substance group *Prilocaine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Prilocaine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Prilocaine hydro...	15230305	21926	60	20150723
Fagron	Prilocaine hydro...	13I02-N03	21048	40	1403257
Fagron	Prilocaine hydro...	13I02-N03	21050	40	20130918
Fagron	Prilocaine hydro...	14H13-B03-297591	21800	60	AR-15-FG-016323-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Prilocaine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 489 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 193 spectra of 4 reference samples from the substance/substance group *Prilocaine hydrochloride*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Prilocaine hydrochloride	15390101	23250	40
Caelo	Prilocaine hydrochloride	15230305	21926SI [†]	60
Caelo	Prilocaine hydrochloride	15390101	23250SI	33
Fagron	Prilocaine hydrochloride	14H13-B03-297591	21800SI [†]	60

- 118 949 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 15 spectra from 10 *Apo-Ident* customers from 14 batches from the substance/substance group *Prilocaine hydrochloride*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Prilocaine hydrochloride	14A03-B34-290281	1
Caelo	Prilocaine hydrochloride	15230304	1
Fagron	Prilocaine hydrochloride	13I032-N03	1
Fagron	Prilocaine hydrochloride	15L21-B02_332956	1
Fagron	Prilocaine hydrochloride	15L21-B02332956	1
Fagron	Prilocaine hydrochloride	17H02-B05-340539	1
Fagron	Prilocaine hydrochloride	15L21-B02-332956	2
Fagron	Prilocaine hydrochloride	15L21-B02325756	1
Fagron	Prilocaine hydrochloride	15E15-B04-307730	1
Fagron	Prilocaine hydrochloride	15L21-B02-319234	1
Fagron	Prilocaine hydrochloride	17H02Bo5348769	1
Fagron	Prilocaine hydrochloride	17H02-B05	1
Fagron	Prilocaine hydrochloride	14H13-B03-297591	1
GEHE 02.05.2013	Prilocaine hydrochloride		1

- 111 232 spectra from 742 *Apo-Ident* customers from a total of 31 877 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Prilocaine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Prilocaine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	188	5	118 949
Type C	0	15	0	111 232

The substance/substance group *Prilocaine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	97.4093 % (> 95.8549 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Prilocaine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Griseofulvin	31.87	—
Atropine sulfate	40.83	—
Glycine	46.68	—
Amphetamine sulfate	48.70	—
Omeprazole	50.97	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Prilocaine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21048	21048	0.00	37.15
21050	21048	1.27	37.58

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21800	21800	0.00	36.78
21926	21800	2.65	39.59

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Procaine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20042-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Procaine hydrochloride; Procaini hydrochloridum

Special notes

When selecting the *Procaine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Procaine hydrochloride	5	4	62

Second-stage model

For differentiation of the substance/substance group *Procaine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Procaine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Procaine hydroch. . .	13109906	21785	60	AR-15-FG-008935-01
Caelo	Procaine hydroch. . .	15006906	22247	60	20150209
Euro OTC	Procaine hydroch. . .	1601014	22306	60	20160203*
Fagron	Procaine hydroch. . .	13F12-B40-301798	22260	60	20141210
Fagron	Procaine hydroch. . .	15J27-B10-322937	23379	40	20151113

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 5 reference samples from the substance/substance group *Procaine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Procaine hydrochloride*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Procaine hydrochloride	161378	22624	40
Caelo	Procaine hydrochloride	171675	23634	40
Caelo	Procaine hydrochloride	182764	24393	40
Caelo	Procaine hydrochloride	190440	24526	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 116 spectra from 83 *Apo-Ident* customers from 64 batches from the substance/substance group *Procaine hydrochloride*.
- Among them are spectra of independent samples from 62 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Procaine hydrochloride	1601014-01	9
Alliance Health 09.09.2...	Procaine hydrochloride	1104012-05	1
Anzag	Procaine hydrochloride	60998058	1
Caelo	Procaine hydrochloride	10159723	1
Caelo	Procaine hydrochloride	10159729	1
Caelo	Procaine hydrochloride	11370203	1
Caelo	Procaine hydrochloride	11370204	1
Caelo	Procaine hydrochloride	11370206	1
Caelo	Procaine hydrochloride	12177801	5
Caelo	Procaine hydrochloride	10159721	1
Caelo	Procaine hydrochloride	11370215	1
Caelo	Procaine hydrochloride	11370219	1
Caelo	Procaine hydrochloride	131099903	1
Caelo	Procaine hydrochloride	13109908	2
Caelo	Procaine hydrochloride	13109915	1
Caelo	Procaine hydrochloride	7011506	1
Caelo	Procaine hydrochloride	13109916	2
Caelo	Procaine hydrochloride	14164408	1
Caelo	Procaine hydrochloride	15006902	1
Caelo	Procaine hydrochloride	15006909	1
Caelo	Procaine hydrochloride	15006912	3
Caelo	Procaine hydrochloride	16137812	3
Caelo	Procaine hydrochloride	16173906	1
Caelo	Procaine hydrochloride	1601014-02	1
Caelo	Procaine hydrochloride	17167504	1
Caelo	Procaine hydrochloride	18041806	1
Caelo	Procaine hydrochloride	17343311	1
Caelo	Procaine hydrochloride	14164413	1
Caelo	Procaine hydrochloride	15006913	1
Caelo	Procaine hydrochloride	11370216	2
Caelo	Procaine hydrochloride	13/09-N08	1
Caelo	Procaine hydrochloride	13F12-B40-302510	1
Caelo	Procaine hydrochloride	60998127	2
Caelo	Procaine hydrochloride	13130-N06	1

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Supplier	Substance	Batch	Spectra
Caelo	Procaine hydrochloride	13109905	1
Caelo	Procaine hydrochloride	17167505	1
Caesar & Loretz GmbH	Procaine hydrochloride	14164413	1
China Medica	Procaine hydrochloride	13109911	1
Euro OTC	Procaine hydrochloride	1003001-02	1
Euro OTC	Procaine hydrochloride	1405027-02	1
Euro OTC	Procaine hydrochloride	1601014-02	13
Euro OTC	Procaine hydrochloride	1601014-02	1
Euro OTC	Procaine hydrochloride	1003001-01	1
Euro OTC	Procaine hydrochloride	1104012-01	1
Euro OTC	Procaine hydrochloride	200644	1
Euro OTC	Procaine hydrochloride	1104012-03	3
Euro OTC	Procaine hydrochloride	1104012-05	4
Euro OTC	Procaine hydrochloride	1104012-04	3
Euro OTC	Procaine hydrochloride	5127	1
Euro OTC	Procaine hydrochloride	16014014-02	1
Euro OTC	Procaine hydrochloride	1405027-01	4
Fagron	Procaine hydrochloride	13/30-N06	1
Fagron	Procaine hydrochloride	15006906	1
Fagron	Procaine hydrochloride	13I09-N08	1
Fagron	Procaine hydrochloride	13F12-B40	1
Fagron	Procaine hydrochloride	1651212	1
Fagron	Procaine hydrochloride	12I10-N07	1
Fagron	Procaine hydrochloride	10H11-N25	1
Gatt-Koller / Phoenix	Procaine hydrochloride	4428/10122714	2
Gehe	Procaine hydrochloride	19044008	1
Herstellung	Procaine hydrochloride	12177801	1
Koisser	Procaine hydrochloride	11370218	1
Noweda	Procaine hydrochloride	1309N08	1
Noweda	Procaine hydrochloride	1601014-02	1
Caelo	Procaine hydrochloride	14164409	1
Phönix 08.01.2014	Procaine hydrochloride	1104012-03	1
Phönix Gotha	Procaine hydrochloride	190311	1
siehe WE-Prüfprotokoll	Procaine hydrochloride	39/12	1
VEB Jenapharmn	Procaine hydrochloride	1011989	1
Caelo	Procaine hydrochloride	13109906	1
Caelo	Procaine hydrochloride	15006906	3

- 111 131 spectra from 742 *Apo-Ident* customers from a total of 31 827 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Procaine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Procaine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	160	0	118 982
Type C	0	113	3	111 131

The substance/substance group *Procaine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	97.4138 % (> 94.8276 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Procaine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ipratropium bromide	48.44	–
Dexamethasone acetate	53.72	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Procaine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21785	21785	0.00	52.43
22247	21785	4.99	53.60
22260	21785	4.35	52.87
22306	22306	0.00	53.81
23379	22306	1.41	52.44

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical

variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Progesterone, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20024-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Progesterone, micronized; Progesteronum micronisatum

Special notes

When selecting the *Progesterone, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Progesterone, micronized	11	35	325

Second-stage model

For differentiation of the substance/substance group *Progesterone, micronized* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Progesterone, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Progesterone, mi...	15319601	22831	40	20151014
Caelo	Progesterone, mi...	17060903	23249	40	20170315
Euro OTC	Progesterone, mi...	1111053-01	20718	30	20120119
Euro OTC	Progesterone, mi...	1506033	21868	60	0000010482
Euro OTC	Progesterone, mi...	1506033	21868SI	30	0000010482
Euro OTC	Progesterone, mi...	1506034	21870	60	0000010483
Euro OTC	Progesterone, mi...	1509008	21907	60	20150914*
Euro OTC	Progesterone, mi...	1511008	22226	60	20151119*
Euro OTC	Progesterone, mi...	1601009	22301	45	20160128*
Euro OTC	Progesterone, mi...	1601009	22301SI	45	20160128*
Euro OTC	Progesterone, mi...	1601001	22303	45	20160128*
Euro OTC	Progesterone, mi...	1603004	22525	40	20160406*
Fagron	Progesterone, mi...	16A20-B02-319103	22830	40	20160209
Fagron	Progesterone, mi...	16A20-B02-319103	22830SI	40	20160209

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 635 spectra of 14 reference samples from the substance/substance group *Progesterone, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.
- 110 054 spectra from a total of 1955 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 2933 spectra of 80 reference samples from the substance/substance group *Progesterone, micronized*.
- Among them are spectra of independent samples from 35 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Progesterone, micronized	170609	23329	40
Caelo	Progesterone, micronized	172778	23838	40
Caelo	Progesterone, micronized	191287	24750	40
Euro OTC	Progesterone, micronized	1603012	22529	40
Euro OTC	Progesterone, micronized	1605013	22556	40
Euro OTC	Progesterone, micronized	1606033	22704	40
Euro OTC	Progesterone, micronized	1605032	22705	40
Euro OTC	Progesterone, micronized	1609016	22788	40
Euro OTC	Progesterone, micronized	1609001	22819	40
Euro OTC	Progesterone, micronized	1701038	23138	40
Euro OTC	Progesterone, micronized	1702026	23148	40
Euro OTC	Progesterone, micronized	1707012	23536	40
Euro OTC	Progesterone, micronized	1705028	23541	40
Euro OTC	Progesterone, micronized	1709012	23732	40
Euro OTC	Progesterone, micronized	1801036	23947	40
Euro OTC	Progesterone, micronized	1802030	24067	40
Euro OTC	Progesterone, micronized	1806020	24138	40
Euro OTC	Progesterone, micronized	1809018	24328	40
Euro OTC	Progesterone, micronized	1809017	24334	40
Euro OTC	Progesterone, micronized	1603012-01	24335	40
Euro OTC	Progesterone, micronized	1811033	24345	40
Euro OTC	Progesterone, micronized	1901021	24447	40
Euro OTC	Progesterone, micronized	1901022	24455	40
Euro OTC	Progesterone, micronized	1904033	24606	40
Euro OTC	Progesterone, micronized	1905023	24765	40
Euro OTC	Progesterone, micronized	1905022	24790	40
Euro OTC	Progesterone, micronized	1908002	24834	40
Euro OTC	Progesterone, micronized	1908003	24863	40
Euro OTC	Progesterone, micronized	1911006	24962	40
Euro OTC	Progesterone, micronized	1911007	24970	40
Euro OTC	Progesterone, micronized	2001036	25077	40
Euro OTC	Progesterone, micronized	2003037	25110	40
Euro OTC	Progesterone, micronized	2003042	25111	40
Euro OTC	Progesterone, micronized	2003036	25112	40
Fagron	Progesterone, micronized	19H20-F02-364866	25046	40
Caelo	Progesterone, micronized	15319601	22831SI [†]	40
Caelo	Progesterone, micronized	17060903	23249SI [†]	20
Caelo	Progesterone, micronized	170609	23329SI	20
Caelo	Progesterone, micronized	172778	23838SI	30
Caelo	Progesterone, micronized	170609	23844	40
Caelo	Progesterone, micronized	170609	23844SI	23
Caelo	Progesterone, micronized	191287	24750SI	40
Euro OTC	Progesterone, micronized	1506033	21868SI [†]	20
Euro OTC	Progesterone, micronized	1506034	21870SI [†]	59
Euro OTC	Progesterone, micronized	1509008	21907SI [†]	53
Euro OTC	Progesterone, micronized	1511008	22226SI [†]	27
Euro OTC	Progesterone, micronized	1601001	22303SI [†]	44
Euro OTC	Progesterone, micronized	1603004	22525SI [†]	31

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Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Progesterone, micronized	1603012	22529SI	29
Euro OTC	Progesterone, micronized	1605013	22556SI	30
Euro OTC	Progesterone, micronized	1606033	22704SI	30
Euro OTC	Progesterone, micronized	1605032	22705SI	38
Euro OTC	Progesterone, micronized	1609016	22788SI	30
Euro OTC	Progesterone, micronized	1609001	22819SI	30
Euro OTC	Progesterone, micronized	1701038	23138SI	20
Euro OTC	Progesterone, micronized	1702026	23148SI	20
Euro OTC	Progesterone, micronized	1707012	23536SI	28
Euro OTC	Progesterone, micronized	1705028	23541SI	25
Euro OTC	Progesterone, micronized	1709012	23732SI	40
Euro OTC	Progesterone, micronized	1801036	23947SI	20
Euro OTC	Progesterone, micronized	1802030	24067SI	32
Euro OTC	Progesterone, micronized	1806020	24138SI	35
Euro OTC	Progesterone, micronized	1809018	24328SI	30
Euro OTC	Progesterone, micronized	1809017	24334SI	40
Euro OTC	Progesterone, micronized	1603012-01	24335SI	20
Euro OTC	Progesterone, micronized	1811033	24345SI	30
Euro OTC	Progesterone, micronized	1901021	24447SI	40
Euro OTC	Progesterone, micronized	1901022	24455SI	40
Euro OTC	Progesterone, micronized	1904033	24606SI	39
Euro OTC	Progesterone, micronized	1905023	24765SI	40
Euro OTC	Progesterone, micronized	1905022	24790SI	40
Euro OTC	Progesterone, micronized	1908002	24834SI	40
Euro OTC	Progesterone, micronized	1908003	24863SI	40
Euro OTC	Progesterone, micronized	1911006	24962SI	40
Euro OTC	Progesterone, micronized	1911007	24970SI	40
Euro OTC	Progesterone, micronized	2001036	25077SI	40
Euro OTC	Progesterone, micronized	2003037	25110SI	40
Euro OTC	Progesterone, micronized	2003042	25111SI	40
Euro OTC	Progesterone, micronized	2003036	25112SI	40
Fagron	Progesterone, micronized	19H20-F02-364866	25046SI	40

- 116 209 spectra from a total of 2377 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1658 spectra from 261 *Apo-Ident* customers from 347 batches from the substance/substance group *Progesterone, micronized*.
- Among them are spectra of independent samples from 325 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H. 03.06.13 ek: 6,50EUR	Progesterone, micronized	1304014-01	1
Euro OTC	Progesterone, micronized	1908002-01	2

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
AHD	Progesterone, micronized	13I11-N11	1
Fagron	Progesterone, micronized	1605013-03	1
Alliance	Progesterone, micronized	15i11-b05-315224	1
Alliance	Progesterone, micronized	15I11-B05-315224	2
Alliance Healthcare	Progesterone, micronized	1206024-02	1
Caelo	Progesterone, micronized	17348402	2
Anzag	Progesterone, micronized	13K28-B01-293478	1
Anzag	Progesterone, micronized	2515A-03235	1
Anzag	Progesterone, micronized	14k11-b04-300921	1
Anzag	Progesterone, micronized	15C31-B06-312963	3
ANZAG	Progesterone, micronized	12195907	2
Anzag 07.04.2016	Progesterone, micronized	APC01-150708P	1
Audor Pharma	Progesterone, micronized	APC01-141212P	1
Audor Pharma	Progesterone, micronized	APC01-150311P	1
Audor Pharma	Progesterone, micronized	APC01-170828P	1
Audor Pharma	Progesterone, micronized	APC01-120613P	1
Audor Pharma	Progesterone, micronized	APC01-160201P	2
Audor Pharma	Progesterone, micronized	APOC01-1700828P	2
Audor Pharma	Progesterone, micronized	APC01-171101P	31
Audor Pharma	Progesterone, micronized	C01-180128	10
Audor Pharma	Progesterone, micronized	APC01-180610P	11
Audor Pharma	Progesterone, micronized	APC01-181003P	12
Audor Pharma	Progesterone, micronized	APC01-160201	1
Audor Pharma	Progesterone, micronized	APC01-150708P	3
Audor Pharma	Progesterone, micronized	C01-120708P	1
Audor Pharma	Progesterone, micronized	APC01-120708P	3
Audor Pharma	Progesterone, micronized	APC01-151114P	4
Caelo	Progesterone, micronized	11177221	2
Caelo	Progesterone, micronized	12195928	7
Caelo	Progesterone, micronized	15I11-B05	1
Caelo	Progesterone, micronized	17149903	1
Caelo	Progesterone, micronized	11177207	1
Caelo	Progesterone, micronized	12195905	3
Caelo	Progesterone, micronized	11177219	3
Caelo	Progesterone, micronized	12195907	4
Caelo	Progesterone, micronized	12195906	4
Caelo	Progesterone, micronized	12195913	3
Caelo	Progesterone, micronized	12195920	8
Caelo	Progesterone, micronized	12195914	3
Caelo	Progesterone, micronized	12195926	19
Caelo	Progesterone, micronized	C01-120613	1
Caelo	Progesterone, micronized	130404002	2
Caelo	Progesterone, micronized	27121303	1
Caelo	Progesterone, micronized	12195902	1
Caelo	Progesterone, micronized	12195828	1
Caelo	Progesterone, micronized	13155927	2
Caelo	Progesterone, micronized	13155920	1
Caelo	Progesterone, micronized	7101401	1
Caelo	Progesterone, micronized	14H13-B05-3002016	1
Caelo	Progesterone, micronized	15319603	42
Caelo	Progesterone, micronized	1511-B05-313598	1
Caelo	Progesterone, micronized	15I11-B05-314184	2
Caelo	Progesterone, micronized	15C31-808	1
Caelo	Progesterone, micronized	4814A-03235	1
Caelo	Progesterone, micronized	15319608	6
Caelo	Progesterone, micronized	16103613	20
Caelo	Progesterone, micronized	16015B14-315279	1
Caelo	Progesterone, micronized	16103606	11
Caelo	Progesterone, micronized	9031705	1
Caelo	Progesterone, micronized	16103604	1

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Supplier	Substance	Batch	Spectra
Caelo	Progesterone, micronized	15319619	1
Caelo	Progesterone, micronized	17060901	41
Caelo	Progesterone, micronized	16J05-B04-328263	1
Caelo	Progesterone, micronized	16103607	1
Caelo	Progesterone, micronized	1605013-02	1
Caelo	Progesterone, micronized	17149906	10
Caelo	Progesterone, micronized	17060907	10
Caelo	Progesterone, micronized	17149907	1
Caelo	Progesterone, micronized	17149904	9
Caelo	Progesterone, micronized	B03333671	1
Caelo	Progesterone, micronized	1719907	10
Caelo	Progesterone, micronized	1760911	1
Caelo	Progesterone, micronized	17277801	22
Caelo	Progesterone, micronized	17060905	1
Caelo	Progesterone, micronized	18B06-B10	2
Caelo	Progesterone, micronized	18098801	25
Caelo	Progesterone, micronized	17348409	3
Caelo	Progesterone, micronized	16L29-B03-330995	1
Caelo	Progesterone, micronized	17C15-B03-333671	1
Caelo	Progesterone, micronized	17060909	6
Caelo	Progesterone, micronized	18B06-B10-346702	1
Caelo	Progesterone, micronized	18F22-B04-351435	1
Caelo	Progesterone, micronized	15319620	1
Caelo	Progesterone, micronized	17348401	1
Caelo	Progesterone, micronized	15124902	1
Caelo	Progesterone, micronized	18f22-B04-354899	1
Caelo	Progesterone, micronized	16103601	2
Caelo	Progesterone, micronized	160100902	1
Caelo	Progesterone, micronized	4817Q-03235	1
Caelo	Progesterone, micronized	13155929	1
Caelo	Progesterone, micronized	13155928	3
Caelo	Progesterone, micronized	14253911	2
Caelo	Progesterone, micronized	15124919	2
Caelo	Progesterone, micronized	1706093	1
Caelo	Progesterone, micronized	18F22-B04-355395	1
Caelo	Progesterone, micronized	12195912	3
Caelo	Progesterone, micronized	258/61	1
Caelo	Progesterone, micronized	15319618	4
Caelo	Progesterone, micronized	12195924	6
Caelo	Progesterone, micronized	13155902	10
Caelo	Progesterone, micronized	14253915	1
Caelo	Progesterone, micronized	15319607	2
Caelo	Progesterone, micronized	EU-HTT160708	1
Caelo	Progesterone, micronized	13HI01-N03	1
Caelo	Progesterone, micronized	HTT140302	1
Caelo	Progesterone, micronized	16103605	2
Caelo	Progesterone, micronized	17/21-B03-343284	1
Caelo	Progesterone, micronized	16A20-B02-319103	1
Caelo	Progesterone, micronized	16D13-B04	1
Caelo	Progesterone, micronized	16103603	11
Caelo	Progesterone, micronized	161036303	9
Caelo	Progesterone, micronized	16103609	30
Caelo	Progesterone, micronized	13155921	2
Caelo	Progesterone, micronized	17348404	7
Caelo	Progesterone, micronized	18263804	7
Caelo	Progesterone, micronized	140100201	1
Caelo	Progesterone, micronized	14K11-B04-300920	2
Caelo	Progesterone, micronized	15124910	3
Caelo	Progesterone, micronized	16103602	4
Caelo	Progesterone, micronized	1721bo3342134	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Progesterone, micronized	17060904	2
Caelo	Progesterone, micronized	1801036-01	16
Caelo	Progesterone, micronized	17348407	4
Caelo	Progesterone, micronized	9195408	1
Caelo	Progesterone, micronized	2006500002	1
Caelo	Progesterone, micronized	16103610	4
Caelo	Progesterone, micronized	19051502	1
Caelo/Gehe	Progesterone, micronized	17060903	2
Caesar & Loretz GmbH	Progesterone, micronized	17348405	1
Caesar & Loretz GmbH	Progesterone, micronized	17060910	1
Caesar & Loretz GmbH	Progesterone, micronized	17348409	1
Caesar & Loretz GmbH	Progesterone, micronized	18263804	1
Caesar u Loretz	Progesterone, micronized	13155920	1
Caesar u Loretz	Progesterone, micronized	15124919	1
Caesar&Lorenz	Progesterone, micronized	16103605	1
Caesar/Noweda	Progesterone, micronized	12195912	1
Caalo/Noweda	Progesterone, micronized	16103607	1
Changzhou Jiaerke Pharma	Progesterone, micronized	1308015-01	1
China Medica	Progesterone, micronized	1308015-01	1
Ebert u. Jacobi 16.0...	Progesterone, micronized	15C31-B06-312963	1
Ebert-Jacobi	Progesterone, micronized	16J05-B04-328263	1
EuRho	Progesterone, micronized	1304040-02	1
EuRho/EuRho	Progesterone, micronized	1904033-01	1
Euro	Progesterone, micronized	1509008-02	1
Euro OTC	Progesterone, micronized	140910-01	1
Euro OTC	Progesterone, micronized	1506033-01	9
Euro OTC	Progesterone, micronized	1304040-01	4
Euro OTC	Progesterone, micronized	1304040-02	3
Euro OTC	Progesterone, micronized	c01-130301	1
Euro OTC	Progesterone, micronized	c01-111218	1
Euro OTC	Progesterone, micronized	1406022-02	2
Euro OTC	Progesterone, micronized	7406022-01	1
Euro OTC	Progesterone, micronized	1409029-1	1
Euro OTC	Progesterone, micronized	1411043-01	4
Euro OTC	Progesterone, micronized	1502030-01	2
Euro OTC	Progesterone, micronized	1509008-01	7
Euro OTC	Progesterone, micronized	15/11-B05-315224	1
Euro OTC	Progesterone, micronized	1609001-01	44
Euro OTC	Progesterone, micronized	1701038-01	30
Euro OTC	Progesterone, micronized	170138-01	20
Euro OTC	Progesterone, micronized	1701038-02	33
Euro OTC	Progesterone, micronized	170103802	9
Euro OTC	Progesterone, micronized	1705028-01	64
Euro OTC	Progesterone, micronized	1704012-01	8
Euro OTC	Progesterone, micronized	1709012-01	99
Euro OTC	Progesterone, micronized	1706009-01	9
Euro OTC	Progesterone, micronized	1801036-01	9
Euro OTC	Progesterone, micronized	18041816	1
Euro OTC	Progesterone, micronized	1801036-02	12
Euro OTC	Progesterone, micronized	1806020-01	55
Euro OTC	Progesterone, micronized	1809017-01	56
Euro OTC	Progesterone, micronized	180901701	20
Euro OTC	Progesterone, micronized	1811033-01	64
Euro OTC	Progesterone, micronized	1901022-01	32
Euro OTC	Progesterone, micronized	1401002-01	3
Euro OTC	Progesterone, micronized	5102	1
Euro OTC	Progesterone, micronized	12195924	1
Euro OTC	Progesterone, micronized	1206024-01	1
Euro OTC	Progesterone, micronized	C01-130301M	1
Euro OTC	Progesterone, micronized	140602202	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Progesterone, micronized	1406910-01	1
Euro OTC	Progesterone, micronized	27061713	1
Euro OTC	Progesterone, micronized	170502801	1
Euro OTC	Progesterone, micronized	1509008_01	1
Euro OTC	Progesterone, micronized	1308015-01	3
Euro OTC	Progesterone, micronized	1211004-01	5
Euro OTC	Progesterone, micronized	1601009-01	10
Euro OTC	Progesterone, micronized	130404001	1
Euro OTC	Progesterone, micronized	C01-130301(M)	2
Euro OTC	Progesterone, micronized	1503033-01	1
Euro OTC	Progesterone, micronized	1409019-01	1
Euro OTC	Progesterone, micronized	160100901	1
Euro OTC	Progesterone, micronized	1509008-02	1
Euro OTC	Progesterone, micronized	1403019-01	2
Euro OTC	Progesterone, micronized	5104	1
Euro OTC	Progesterone, micronized	1605013-03	4
Euro/ Sanacorp	Progesterone, micronized	C01-131116(M)	1
Euro OTC	Progesterone, micronized	1503012-01	6
Euro OTC	Progesterone, micronized	1605013-01	21
Euro OTC	Progesterone, micronized	1605013-02	43
Euro OTC	Progesterone, micronized	160501303	2
Euro OTC	Progesterone, micronized	1809017-02	1
Europh-Jenne	Progesterone, micronized	1406022-01	1
Fagron	Progesterone, micronized	18B06-B10	2
Fagron	Progesterone, micronized	12D05-N06	3
Fagron	Progesterone, micronized	1910213235	1
Fagron	Progesterone, micronized	12G05-N17	6
Fagron	Progesterone, micronized	12K05-N01	2
Fagron	Progesterone, micronized	13A02N01	1
Fagron	Progesterone, micronized	12K05-N07	1
Fagron	Progesterone, micronized	13A02-N01	3
Fagron	Progesterone, micronized	13G11-N02	6
Fagron	Progesterone, micronized	13I11-N11	2
Fagron	Progesterone, micronized	C01-130301	1
Fagron	Progesterone, micronized	13H01-N03	7
Fagron	Progesterone, micronized	12A19-N04	1
Fagron	Progesterone, micronized	13K-B30-288261	1
Fagron	Progesterone, micronized	1311-N11	1
Fagron	Progesterone, micronized	13K28-B30-288261	1
Fagron	Progesterone, micronized	14C10B0129347	1
Fagron	Progesterone, micronized	14D22-B04	2
Fagron	Progesterone, micronized	14c10-B01-293478	1
Fagron	Progesterone, micronized	14c10-b01-293478	1
Fagron	Progesterone, micronized	13h01-n03	1
Fagron	Progesterone, micronized	14D22-B04-293477	1
Fagron	Progesterone, micronized	14C10-B01	1
Fagron	Progesterone, micronized	14D22-B293479	1
Fagron	Progesterone, micronized	HTT140207	1
Fagron	Progesterone, micronized	14K11-B04	3
Fagron	Progesterone, micronized	14L15-B05-302292	2
Fagron	Progesterone, micronized	14k11-b04	1
Fagron	Progesterone, micronized	15C31-B06-309790	2
Fagron	Progesterone, micronized	15C31-B06	2
Fagron	Progesterone, micronized	HTT150201	3
Fagron	Progesterone, micronized	15B12-Bo4-304838	1
Fagron	Progesterone, micronized	15C31-B06-308439	7
Fagron	Progesterone, micronized	HTT140413	1
Fagron	Progesterone, micronized	15B12-B04-304837	2
Fagron	Progesterone, micronized	15I11-B05-314842	1
Fagron	Progesterone, micronized	15C31-B06-313599	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Progesterone, micronized	HTT140503	1
Fagron	Progesterone, micronized	200650-315224	1
Fagron	Progesterone, micronized	16A20-B02-321375	2
Fagron	Progesterone, micronized	15I11-B05	1
Fagron	Progesterone, micronized	1511-805	1
Fagron	Progesterone, micronized	1511B05-315224	1
Fagron	Progesterone, micronized	16G15-B04-325279	5
Fagron	Progesterone, micronized	16G15-B04325279	1
Fagron	Progesterone, micronized	16G15-B04-325755	2
Fagron	Progesterone, micronized	15I11-B05-313598	1
Fagron	Progesterone, micronized	16G15-B04-325135	1
Fagron	Progesterone, micronized	16g115-b04-325136	1
Fagron	Progesterone, micronized	16G15-B04325136	1
Fagron	Progesterone, micronized	16J05-B04-328303	2
Fagron	Progesterone, micronized	16G15B04-325279	1
Fagron	Progesterone, micronized	16g15-b04	1
Fagron	Progesterone, micronized	16G15-B04-325136	3
Fagron	Progesterone, micronized	16G15-B04	2
Fagron	Progesterone, micronized	200650-0004	2
Fagron	Progesterone, micronized	16L29-B03-332060	5
Fagron	Progesterone, micronized	17C15-B03-333672	2
Fagron	Progesterone, micronized	17C15-B03-333671	3
Fagron	Progesterone, micronized	17C15B03333671	2
Fagron	Progesterone, micronized	17D25-B06-339655	2
Fagron	Progesterone, micronized	16L29-B-332061	1
Fagron	Progesterone, micronized	17/21-B03-341517	1
Fagron	Progesterone, micronized	17I21-803	1
Fagron	Progesterone, micronized	17I21-B03-342135	1
Fagron	Progesterone, micronized	17I21-B03-343284	2
Fagron	Progesterone, micronized	17I08-B04	1
Fagron	Progesterone, micronized	ApC01-180128P	1
Fagron	Progesterone, micronized	17I08-B04-344773	1
Fagron	Progesterone, micronized	18B06-B10-347484	4
Fagron	Progesterone, micronized	C01-171216	1
Fagron	Progesterone, micronized	18B06-B10-349775	3
Fagron	Progesterone, micronized	17I21-B03-341516	1
Fagron	Progesterone, micronized	18F22-B04-351145	3
Fagron	Progesterone, micronized	18F22-B04-351435	2
Fagron	Progesterone, micronized	18F22-B04-354900	2
Fagron	Progesterone, micronized	18F22-B04-355395	1
Fagron	Progesterone, micronized	19A25-B01-360449	3
Fagron	Progesterone, micronized	14022-B04-293476	1
Fagron	Progesterone, micronized	16L29-B03-332505	4
Fagron	Progesterone, micronized	13/11-N11	1
Fagron	Progesterone, micronized	15C31-B06-308796	4
Fagron	Progesterone, micronized	EU-HTT160502	1
Fagron	Progesterone, micronized	16L29-B03-302060	1
Fagron	Progesterone, micronized	C01-170814	1
Fagron	Progesterone, micronized	18F22-B04-351998	1
Fagron	Progesterone, micronized	19H20-F02-364867	1
Fagron	Progesterone, micronized	C01-120322	1
Fagron	Progesterone, micronized	13k28-b30-288261	1
Fagron	Progesterone, micronized	16129b03332060	1
Fagron	Progesterone, micronized	18B06-B10-346701	4
Fagron	Progesterone, micronized	13AC2-N01	1
Fagron	Progesterone, micronized	14K11-B04_300921	1
Fagron	Progesterone, micronized	14K11-B04-300920	6
Fagron	Progesterone, micronized	20170427Ma6	1
Fagron	Progesterone, micronized	intern20180619Ma3	1
Fagron	Progesterone, micronized	18F22-B04353582-P201	1

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Supplier	Substance	Batch	Spectra
Fagron	Progesterone, micronized	17I21-B03-341520	1
Fagron	Progesterone, micronized	1511-B05-314842	1
Fagron	Progesterone, micronized	17/21-B03-343284	2
Fagron	Progesterone, micronized	17/21-B03-342135	2
Fagron	Progesterone, micronized	13K28-B30-288262	1
Fagron	Progesterone, micronized	16A20-B02-321373	2
Fagron	Progesterone, micronized	16a20-b02-318667	1
Fagron	Progesterone, micronized	5013I-03235	1
Fagron	Progesterone, micronized	16a20-b02-321375	1
Fagron	Progesterone, micronized	16D13-B04-323636	1
Fagron	Progesterone, micronized	16111-B04-314184	1
Fagron	Progesterone, micronized	18F22-B04-353582	2
Fagron	Progesterone, micronized	16L29-B03	1
Fagron	Progesterone, micronized	19H20-F02	2
Fagron	Progesterone, micronized	16A20-B02-321374	4
Fagron	Progesterone, micronized	16A20-B02-318667	3
Fagron	Progesterone, micronized	15C31-B06-312963	1
Fagron	Progesterone, micronized	16L29-B03-330995	1
Fagron	Progesterone, micronized	17D25-B06-339651	1
Fagron	Progesterone, micronized	18B06-B10-346702	1
Fagron	Progesterone, micronized	18F22-B04-352735	1
Fagron	Progesterone, micronized	EU-HTT160705	2
Fagron	Progesterone, micronized	18F22_B04_354899	1
Fagron	Progesterone, micronized	16g15-b04-326487	1
Fagron	Progesterone, micronized	1-111218	1
Fagron	Progesterone, micronized	17d25-b06	1
Fagron	Progesterone, micronized	19H20-F02-364866	1
Fagron	Progesterone, micronized	13b08-n01	1
Fagron	Progesterone, micronized	12k05-n07	1
Fagron	Progesterone, micronized	14C10-B01-293478	2
Fagron	Progesterone, micronized	HTT140302	1
Fagron	Progesterone, micronized	160A20-B02-321373	1
Fagron	Progesterone, micronized	16G15-B04-32579	1
Fagron	Progesterone, micronized	16J05-B04-328263	3
Fagron	Progesterone, micronized	17/21-B03-341518	1
Fagron	Progesterone, micronized	17I21-B03	1
Fagron	Progesterone, micronized	18806-B10-349153	1
Fagron	Progesterone, micronized	14D22-Bo4	1
Fagron	Progesterone, micronized	375779	1
Fagron	Progesterone, micronized	17C15-B03-333671	1
Fagron	Progesterone, micronized	15I11-B05-314184	4
Fagron	Progesterone, micronized	1511-B05-314184	1
Fagron	Progesterone, micronized	14K11-B04-300921	1
Fagron	Progesterone, micronized	16G15-B04-326487	3
Fagron	Progesterone, micronized	17I21-B03-341518	1
Fagron	Progesterone, micronized	1721B03342134	1
Fagron	Progesterone, micronized	18F22-B04	1
Fagron	Progesterone, micronized	14D22-B04-293476	1
Fagron	Progesterone, micronized	14K11B04300920	1
Fagron	Progesterone, micronized	15C31-Bo6-308796	1
Fagron	Progesterone, micronized	15C31B06308439	1
Fagron	Progesterone, micronized	15C31-B06-308786	1
Fagron	Progesterone, micronized	15C31-B06-316105	3
Fagron	Progesterone, micronized	15I11-B05-315224	2
Fagron	Progesterone, micronized	15/11-B05-315224	2
Fagron	Progesterone, micronized	18F22-B04-354899	3
Fiebig	Progesterone, micronized	17I21-B03	1
Fiebig	Progesterone, micronized	17060909	1
Fragon	Progesterone, micronized	13A02-N02	1
fragon	Progesterone, micronized	16A20-B02-319103	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Progesterone, micronized	1601009-02	4
Caelo	Progesterone, micronized	13G11-N02	1
keine Angabe	Progesterone, micronized	1304040-01	1
Klenk	Progesterone, micronized	C01-120322	1
Kögl	Progesterone, micronized	1802398	1
L12	Progesterone, micronized	1605013-01	1
L12	Progesterone, micronized	17060909	2
L30	Progesterone, micronized	17060910	1
L30	Progesterone, micronized	18B06-B10-349775	1
Caelo	Progesterone, micronized	12A19-N04	2
Fagron	Progesterone, micronized	14H13-B05-300216	7
Euro OTC	Progesterone, micronized	1406022-01	1
Euro OTC	Progesterone, micronized	141104301	1
Euro OTC	Progesterone, micronized	1409029-01	5
Euro OTC	Progesterone, micronized	1705028	1
Euro OTC	Progesterone, micronized	HTT160102	1
Euro OTC	Progesterone, micronized	co1-111218(M)	1
Euro OTC	Progesterone, micronized	17I08-B04	1
PHOENIX am 18.03.2014	Progesterone, micronized	13A02-N01	1
Phoenix 09.12.14	Progesterone, micronized	13H01-N03	1
Phoenix 28.03.2014	Progesterone, micronized	13G11-N02	1
Phoenix/Cealo	Progesterone, micronized	17/21-B03-341517	1
phönix	Progesterone, micronized	16g15-b04-326487	1
Phönix	Progesterone, micronized	13155920	1
Phönix	Progesterone, micronized	15319604	1
Phönix	Progesterone, micronized	16A20-B02-319103	1
Phönix	Progesterone, micronized	1605013-01	1
Caelo	Progesterone, micronized	17060911	2
sanacorp	Progesterone, micronized	15124902	1
Sanacorp	Progesterone, micronized	12195914	1
Sanacorp	Progesterone, micronized	12195928	1
Sanacorp	Progesterone, micronized	13A02-N01	1
Sanacorp	Progesterone, micronized	13155902	1
Sanacorp	Progesterone, micronized	15/11-B05-315224	3
Sanacorp	Progesterone, micronized	14C10-B01-293478	1
Sanacorp	Progesterone, micronized	17D25-B06	1
Sanacorp	Progesterone, micronized	1809017-01	1
Caelo	Progesterone, micronized	14253929	1
Caelo	Progesterone, micronized	15319602	1
Caelo	Progesterone, micronized	9195429	1
Fagron	Progesterone, micronized	17/21-B03-342134	1
VDL;07.11.14;39,95 euro	Progesterone, micronized	13155921	1
	Progesterone, micronized	1401002-01	2
Caelo	Progesterone, micronized	15319601	5
Caelo	Progesterone, micronized	17060903	3
Euro OTC	Progesterone, micronized	1111053-01	6
Euro OTC	Progesterone, micronized		2
Fagron	Progesterone, micronized	16A20-B02-319103	1
Fagron	Progesterone, micronized		2
	Progesterone, micronized	14253906	1
Vdl 28.04.14;Preis 39,95	Progesterone, micronized		1

- 109 589 spectra from 742 *Apo-Ident* customers from a total of 31 547 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Progesterone, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Progesterone, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	635	0	110 054
Type B	0	2933	0	116 209
Type C	0	1654	4	109 589

The substance/substance group *Progesterone, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0551 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.7954 %)
Type C	100.0000 % (> 99.8899 %)	99.7587 % (> 99.5778 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Progesterone, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Testosterone propionate	10.46	46.39
Povidone iodine	38.12	—
Budesonide, micronized	39.31	—
Spirolactone	41.82	36.39
Norethisterone acetate	42.54	—
Estradiol valerate	44.63	—
Finasteride (form III)	48.72	—
⋮	⋮	⋮
Estriol	>50	75.15
Pregnenolone	>50	137.58
Alfatradiol	>50	181.79
Quinine hydrochloride	>50	335.73
Quinine sulfate	>50	425.48

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Progesterone, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20718	22303	2.65	13.99
22303	22303	0.00	12.55
21907	21907	0.00	14.39
22301	22301	0.00	11.85
21868	21868	0.00	14.01
22226	22226	0.00	13.07
22831	22301	2.65	14.97
21870	21870	0.00	14.98
22525	22525	0.00	14.59
22830	21907	2.28	16.49
23249	22303	3.24	14.38

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Promethazine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20208-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Promethazine hydrochloride; Promethazini hydrochloridum

Special notes

When selecting the *Promethazine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Promethazine hydrochloride	2	2	4

Second-stage model

For differentiation of the substance/substance group *Promethazine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Promethazine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Promethazine hyd. ...	13119214	21690	60	20130506
Caelo	Promethazine hyd. ...	161466	22628	40	20160621*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 100 spectra of 2 reference samples from the substance/substance group *Promethazine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 589 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Promethazine hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Promethazine hydrochloride	17058601	23248	40
Caelo	Promethazine hydrochloride	170586	23324	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 4 *Apo-Ident* customers from 4 batches from the substance/substance group *Promethazine hydrochloride*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Promethazine hydrochloride	11352305	1
Caelo	Promethazine hydrochloride	19051805	1
Caelo	Promethazine hydrochloride	17058601	1
Caelo	Promethazine hydrochloride	13119211	1

- 111 243 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Promethazine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Promethazine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	100	0	110 589
Type B	0	80	0	119 062
Type C	0	4	0	111 243

The substance/substance group *Promethazine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Promethazine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Pheniramine maleate	35.81	—
Methadone hydrochloride	46.88	—
Diltiazem hydrochloride	52.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Promethazine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21690	22628	2.35	56.02
22628	22628	0.00	58.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Propranolol hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20954-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Propranolol hydrochloride; Propranololi hydrochloridum

Special notes

When selecting the *Propranolol hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Propranolol hydrochloride	4	3	110

Second-stage model

For differentiation of the substance/substance group *Propranolol hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Propranolol hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Propranolol hydr...	12370712	21396	60	20130116
Caelo	Propranolol hydr...	12370712	21410	60	20130116
Caelo	Propranolol hydr...	15283302	22590	40	20150929
Fagron	Propranolol hydr...	13I13-N04	20954	40	1402307
Fagron	Propranolol hydr...	15F16-B02-312979	22591	40	20150630

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Propranolol hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Propranolol hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Propranolol hydrochloride	171722	23650	40
Caelo	Propranolol hydrochloride	173330	23836	40
Caelo	Propranolol hydrochloride	192472	24878	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 496 spectra from 254 *Apo-Ident* customers from 123 batches from the substance/substance group *Propranolol hydrochloride*.
- Among them are spectra of independent samples from 108 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
/O. Geilenkirchen	Propranolol hydrochloride	15422502	1
AHD	Propranolol hydrochloride	15422501	1
AHD	Propranolol hydrochloride	941895	1
AHD	Propranolol hydrochloride	17172204	2
AHD	Propranolol hydrochloride	17333001	1
AHD	Propranolol hydrochloride	17333006	1
AHD	Propranolol hydrochloride	18179402	3
Alliance health	Propranolol hydrochloride	13E15-B40-294297	1
allianz	Propranolol hydrochloride	15283302	1
Caelo	Propranolol hydrochloride	17K22-B03-345013	4
Audor Pharma	Propranolol hydrochloride	15K11-B01	1
Caelo	Propranolol hydrochloride	12370709	1
Caelo	Propranolol hydrochloride	13I13N04	1
Caelo	Propranolol hydrochloride	13379806	1
Caelo	Propranolol hydrochloride	15F16-B02	1
Caelo	Propranolol hydrochloride	13379804	1
Caelo	Propranolol hydrochloride	15082404	1
Caelo	Propranolol hydrochloride	15082405	2
Caelo	Propranolol hydrochloride	15283301	11
Caelo	Propranolol hydrochloride	2771	1
Caelo	Propranolol hydrochloride	15422502	14
Caelo	Propranolol hydrochloride	154225	1
Caelo	Propranolol hydrochloride	15k11-B01	1
Caelo	Propranolol hydrochloride	16E09-B09-330547	4
Caelo	Propranolol hydrochloride	150082405	1
Caelo	Propranolol hydrochloride	17172203	15
Caelo	Propranolol hydrochloride	16138306	2
Caelo	Propranolol hydrochloride	17172204	11
Caelo	Propranolol hydrochloride	17172205	5
Caelo	Propranolol hydrochloride	17333001	17
Caelo	Propranolol hydrochloride	17333005	1
Caelo	Propranolol hydrochloride	17K22-B03-344247	1
Caelo	Propranolol hydrochloride	1733301	2
Caelo	Propranolol hydrochloride	17333006	5
Caelo	Propranolol hydrochloride	17K22-B03-342731	1

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Supplier	Substance	Batch	Spectra
Caelo	Propranolol hydrochloride	18179402	24
Caelo	Propranolol hydrochloride	18D23-B09-355583	3
Caelo	Propranolol hydrochloride	18179403	6
Caelo	Propranolol hydrochloride	13379809	3
Caelo	Propranolol hydrochloride	1712203	1
Caelo	Propranolol hydrochloride	12370710	1
Caelo	Propranolol hydrochloride	15082401	4
Caelo	Propranolol hydrochloride	15422505	7
Caelo	Propranolol hydrochloride	15K11-B01-316401	1
Caelo	Propranolol hydrochloride	16138304	11
Caelo	Propranolol hydrochloride	173330015654	1
Caelo	Propranolol hydrochloride	15F16-B02-312979	3
Caelo	Propranolol hydrochloride	M141203	1
Caelo	Propranolol hydrochloride	16E09-B09-326637	1
Caelo	Propranolol hydrochloride	1712204	1
Caelo	Propranolol hydrochloride	m130104	1
Caelo	Propranolol hydrochloride	12370703	1
Caelo	Propranolol hydrochloride	12D27-N14	1
Caelo	Propranolol hydrochloride	13/13-N04	3
Caelo	Propranolol hydrochloride	15422501	12
Caelo	Propranolol hydrochloride	13379807	5
Caelo	Propranolol hydrochloride	18D23-B09-351774	6
Caelo	Propranolol hydrochloride	15179405	1
Caelo	Propranolol hydrochloride	1542251	1
Caelo	Propranolol hydrochloride	16138302	7
Caelo	Propranolol hydrochloride	17K22-B03-347251	2
Caelo	Propranolol hydrochloride	18179405	4
Caelo/Noweda	Propranolol hydrochloride	15283302	1
Caesar & Loretz GmbH	Propranolol hydrochloride	18179402	4
Caesar & Loretz GmbH	Propranolol hydrochloride	18179403	2
Caesar & Loretz GmbH / ...	Propranolol hydrochloride	15422502	1
Caesar u Loretz	Propranolol hydrochloride	13379807	1
Calo/AHD	Propranolol hydrochloride	15082401	1
Caselo	Propranolol hydrochloride	18179405	1
Changzhou Yabang Pharma...	Propranolol hydrochloride	15F16-B02	1
Euro OTC	Propranolol hydrochloride	15K11-B01-322717	1
Euro OTC	Propranolol hydrochloride	13379806	1
Euro OTC	Propranolol hydrochloride	13I13-N04	1
Euro OTC	Propranolol hydrochloride	15K11B01-320607	1
Euro OTC	Propranolol hydrochloride	16138304	2
Fagron	Propranolol hydrochloride	15F16-B02	1
Fagron	Propranolol hydrochloride	12D27-N14	4
Fagron	Propranolol hydrochloride	31101201	1
Fagron	Propranolol hydrochloride	12A27-N04	1
Fagron	Propranolol hydrochloride	20250711-8	1
Fagron	Propranolol hydrochloride	402310015	1
Fagron	Propranolol hydrochloride	12K06-N07	7
Fagron	Propranolol hydrochloride	11I19-N09	1
Fagron	Propranolol hydrochloride	12K06N07	1
Fagron	Propranolol hydrochloride	13I3-N04	2
Fagron	Propranolol hydrochloride	3050PRRII	2
Fagron	Propranolol hydrochloride	9CMK6AA71374	1
Fagron	Propranolol hydrochloride	13E15-B40-289355	10
Fagron	Propranolol hydrochloride	4071401	1
Fagron	Propranolol hydrochloride	13E15-B40	5
Fagron	Propranolol hydrochloride	28051508	1
Fagron	Propranolol hydrochloride	13E15_B40-297021	1
Fagron	Propranolol hydrochloride	M130104	1
Fagron	Propranolol hydrochloride	15K11-Bo1-316401	1
Fagron	Propranolol hydrochloride	15K11-B01-322717	4

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Supplier	Substance	Batch	Spectra
Fagron	Propranolol hydrochloride	10L20N08	2
Fagron	Propranolol hydrochloride	16E09-B09-326637	15
Fagron	Propranolol hydrochloride	M141203	1
Fagron	Propranolol hydrochloride	15K11-B01-16401	1
Fagron	Propranolol hydrochloride	16E09-B09	2
Fagron	Propranolol hydrochloride	18041807	1
Fagron	Propranolol hydrochloride	17K22-B03-350048	3
Fagron	Propranolol hydrochloride	18D23-B09-357778	1
Fagron	Propranolol hydrochloride	17K22-b03-350048	1
Fagron	Propranolol hydrochloride	16E09-B09-330547	6
Fagron	Propranolol hydrochloride	M170602	2
Fagron	Propranolol hydrochloride	13113-N04	1
Fagron	Propranolol hydrochloride	16138302	1
Fagron	Propranolol hydrochloride	17K22-B03-342731	7
Fagron	Propranolol hydrochloride	12F29-N06	4
Fagron	Propranolol hydrochloride	15K11_B01_322717	1
Fagron	Propranolol hydrochloride	3050PRII	1
Fagron	Propranolol hydrochloride	17K-22-B03-345013	1
Fagron	Propranolol hydrochloride	5101	1
Fagron	Propranolol hydrochloride	18D23-B09	4
Fagron	Propranolol hydrochloride	11L01-N05	2
Fagron	Propranolol hydrochloride	13/13-N04	4
Fagron	Propranolol hydrochloride	9L09-N06	1
Fagron	Propranolol hydrochloride	12F29-N06	1
Fagron	Propranolol hydrochloride	16E09-B09333442	1
Fagron	Propranolol hydrochloride	13E15-B40-297021	6
Fagron	Propranolol hydrochloride	15K11-B01-316401	12
Fagron	Propranolol hydrochloride	13E15-B40-294297	5
Fagron	Propranolol hydrochloride	16E09-B09-333442	11
Fagron	Propranolol hydrochloride	17k22-b03-347251	1
Fagron	Propranolol hydrochloride	3913M-03609	1
Fagron	Propranolol hydrochloride	15K11-B01	3
Fagron	Propranolol hydrochloride	17K22-B03-347251	3
Fagron	Propranolol hydrochloride	M151204	1
Fagron	Propranolol hydrochloride	17K22-B03-344247	3
Fagron	Propranolol hydrochloride	18D23-B09-355583	3
Fagron	Propranolol hydrochloride	18D23-B09-359713	1
Fagron	Propranolol hydrochloride	3112U-03609	1
Fagron	Propranolol hydrochloride	18D23-B09-351774	4
Fagron	Propranolol hydrochloride	13J13-N04	3
Fargon	Propranolol hydrochloride	12K06-N07	1
Fargon	Propranolol hydrochloride	M140808	1
Fargon	Propranolol hydrochloride	18D23-B09	1
fragon/AHD	Propranolol hydrochloride	13/13-N04	1
Gehe	Propranolol hydrochloride	16E09-B09	1
Gehe	Propranolol hydrochloride	17172203	1
Gehe	Propranolol hydrochloride	17172205	2
GEHE	Propranolol hydrochloride	18179405	1
Gehe Kassel 26.06.2015	Propranolol hydrochloride	15082401	1
Caelo	Propranolol hydrochloride	M130104	1
Fagron	Propranolol hydrochloride	11D01-N11	1
Fagron	Propranolol hydrochloride	15K11-B01-320607	8
Gutenberg-Apotheke	Propranolol hydrochloride	13I13-N04	1
InfectoPharm	Propranolol hydrochloride	J0512011	1
Inresa 22.09.15	Propranolol hydrochloride	3043PRRII	1
Jenne	Propranolol hydrochloride	17333001	1
JENNE	Propranolol hydrochloride	17333001	1
L12	Propranolol hydrochloride	16E09-B09-326637	1
L12	Propranolol hydrochloride	17K22-B03-350048	1
L12	Propranolol hydrochloride	18D23-B09-355583	1

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Supplier	Substance	Batch	Spectra
L30	Propranolol hydrochloride	15K11-B01-320607	1
Löwen City-Apotheke Bar...	Propranolol hydrochloride	4012013	1
Noweda	Propranolol hydrochloride	18179402	1
Noweda/Apomix	Propranolol hydrochloride	15K11-B01-316401	1
Fagron	Propranolol hydrochloride	700556-0001	1
Fagron	Propranolol hydrochloride	17K22-B03	2
Phoenix	Propranolol hydrochloride	17K22-B03-344247	1
Phoenix	Propranolol hydrochloride	18179402	1
Phoenix	Propranolol hydrochloride	18D23-B09-355583	1
Phoenix/Fargron	Propranolol hydrochloride	15K11-B01-322717	2
phönix	Propranolol hydrochloride	2/AKD3	1
phönix	Propranolol hydrochloride	16e09b09326637	1
phönix	Propranolol hydrochloride	16e09-b09	1
Phönix	Propranolol hydrochloride	15k11-b01-322717	1
Phönix	Propranolol hydrochloride	16E09-B09-326637	1
Phönix	Propranolol hydrochloride	17172203	1
Fagron	Propranolol hydrochloride	15F16B02312979	1
Fagron	Propranolol hydrochloride	17K22-B03-30048	1
Sanacorp	Propranolol hydrochloride	12370712	1
Sanacorp	Propranolol hydrochloride	16138304	1
Sanacorp	Propranolol hydrochloride	18D23-B09-351774	1
Caelo	Propranolol hydrochloride	13E15-B40-289355	2
Caelo	Propranolol hydrochloride	12a27-n04	1
VDL	Propranolol hydrochloride	18D23-B09-359713	1
WE:Phönix 12.08.2016	Propranolol hydrochloride	15422502	1
Caelo	Propranolol hydrochloride	15283302	5
Caelo	Propranolol hydrochloride	12370712	1
Fagron	Propranolol hydrochloride	13I13-N04	8
Fagron	Propranolol hydrochloride		2
Fagron	Propranolol hydrochloride	15F16-B02-312979	4
Gehe	Propranolol hydrochloride		1
Noweda	Propranolol hydrochloride		1

- 110 751 spectra from 742 *Apo-Ident* customers from a total of 31 768 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Propranolol hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Propranolol hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	120	0	119 022
Type C	0	454	42	110 751

The substance/substance group *Propranolol hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	91.5323 % (> 90.9274 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Propranolol hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Naphazoline nitrate	46.00	—
Phenylephrine hydrochloride	59.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Propranolol hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20954	20954	0.00	57.03
21396	20954	2.21	53.58
21410	20954	16.82	57.47
22590	20954	7.24	59.78
22591	20954	15.57	55.24

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Propyl-4-hydroxybenzoate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20981-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Propyl-4-hydroxybenzoate; Propylis parahydroxybenzoas

Special notes

When selecting the *Propyl-4-hydroxybenzoate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Propyl-4-hydroxybenzoate	4	1	54

Second-stage model

For differentiation of the substance/substance group *Propyl-4-hydroxybenzoate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Propyl-4-hydroxybenzoate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Propyl-4-hydroxy...	11373523	20981	40	1402440
Caelo	Propyl-4-hydroxy...	13365009	21758	60	20131203
Caelo	Propyl-4-hydroxy...	162595	22754	40	20161005*
Caelo	Propyl-4-hydroxy...	162595	22765	40	20161005*
Caelo	Propyl-4-hydroxy...	190732	24497	40	20190404*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Propyl-4-hydroxybenzoate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Propyl-4-hydroxybenzoate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Propyl-4-hydroxybenzoate	171970	23675	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 162 spectra from 115 *Apo-Ident* customers from 56 batches from the substance/substance group *Propyl-4-hydroxybenzoate*.
- Among them are spectra of independent samples from 54 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Propyl-4-hydroxybenzoate	11373523	1
Caelo	Propyl-4-hydroxybenzoate	14359009	1
Anzag	Propyl-4-hydroxybenzoate	11373512	2
Caelo	Propyl-4-hydroxybenzoate	113735223	1
Caelo	Propyl-4-hydroxybenzoate	3041408	1
Caelo	Propyl-4-hydroxybenzoate	13100208	1
Caelo	Propyl-4-hydroxybenzoate	13051504	1
Caelo	Propyl-4-hydroxybenzoate	1108211931	1
Caelo	Propyl-4-hydroxybenzoate	11102624	1
Caelo	Propyl-4-hydroxybenzoate	11373512	3
Caelo	Propyl-4-hydroxybenzoate	11102611	2
Caelo	Propyl-4-hydroxybenzoate	713Q-01931	1
Caelo	Propyl-4-hydroxybenzoate	11102609	1
Caelo	Propyl-4-hydroxybenzoate	11373524	1
Caelo	Propyl-4-hydroxybenzoate	82792159	1
Caelo	Propyl-4-hydroxybenzoate	13100218	2
Caelo	Propyl-4-hydroxybenzoate	13365011	5
Caelo	Propyl-4-hydroxybenzoate	13100219	1
Caelo	Propyl-4-hydroxybenzoate	14359005	8
Caelo	Propyl-4-hydroxybenzoate	15246501	1
Caelo	Propyl-4-hydroxybenzoate	14359019	1
Caelo	Propyl-4-hydroxybenzoate	15246502	2
Caelo	Propyl-4-hydroxybenzoate	16359006	1
Caelo	Propyl-4-hydroxybenzoate	16259505	9
Caelo	Propyl-4-hydroxybenzoate	16259516	12
Caelo	Propyl-4-hydroxybenzoate	11121709	1
Caelo	Propyl-4-hydroxybenzoate	17343108	1
Caelo	Propyl-4-hydroxybenzoate	17343110	6
Caelo	Propyl-4-hydroxybenzoate	14359008	22
Caelo	Propyl-4-hydroxybenzoate	13100215	7
Caelo	Propyl-4-hydroxybenzoate	19073203	2
Caelo	Propyl-4-hydroxybenzoate	11373505	1
Caelo	Propyl-4-hydroxybenzoate	14359020	4
Caelo	Propyl-4-hydroxybenzoate	113735	1
Caelo	Propyl-4-hydroxybenzoate	14359006	3
Caelo	Propyl-4-hydroxybenzoate	17343101	7
Caelo	Propyl-4-hydroxybenzoate	1913I-01931	1

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Supplier	Substance	Batch	Spectra
Caelo	Propyl-4-hydroxybenzoate	4314U-01931	1
Caelo	Propyl-4-hydroxybenzoate	3115M-01931	1
Caelo	Propyl-4-hydroxybenzoate	13100217	3
Caelo	Propyl-4-hydroxybenzoate	11373518	2
Caelo	Propyl-4-hydroxybenzoate	13365006	5
Caelo	Propyl-4-hydroxybenzoate	15276514	2
Caelo	Propyl-4-hydroxybenzoate	17343105	1
Caesar & Loretz GmbH	Propyl-4-hydroxybenzoate	13100215	1
Caesar/Noweda	Propyl-4-hydroxybenzoate	3710M-01931	2
Euro OTC	Propyl-4-hydroxybenzoate	2509025	1
Fagron	Propyl-4-hydroxybenzoate	610M-01931	1
Fagron	Propyl-4-hydroxybenzoate	12B13-N04	1
Gatt-Koller	Propyl-4-hydroxybenzoate	1800302	1
GATT-KOLLER/PHOENIX	Propyl-4-hydroxybenzoate	5080/11130214	1
Gehe 5.3.14	Propyl-4-hydroxybenzoate	13100215	1
Caelo	Propyl-4-hydroxybenzoate	13365012	2
Caelo	Propyl-4-hydroxybenzoate	290114PML03	1
Caelo	Propyl-4-hydroxybenzoate	221014PAS01	1
Noweda	Propyl-4-hydroxybenzoate	11373505	1
Noweda	Propyl-4-hydroxybenzoate	14359005	1
Noweda	Propyl-4-hydroxybenzoate	14359020	1
Noweda	Propyl-4-hydroxybenzoate	17343101	1
Phoenix	Propyl-4-hydroxybenzoate	13100215	1
Phoenix	Propyl-4-hydroxybenzoate	19073203	1
PHOENIX 10.03.2014	Propyl-4-hydroxybenzoate	11373526	1
Phönix	Propyl-4-hydroxybenzoate	17343108	1
Phönix 14.01.2014	Propyl-4-hydroxybenzoate	11373526	1
Sanacorp	Propyl-4-hydroxybenzoate	AKD3	1
Sanacorp	Propyl-4-hydroxybenzoate	16259516	1
siehe WE-Prüfprotokoll	Propyl-4-hydroxybenzoate	84/11	1
Caelo	Propyl-4-hydroxybenzoate	11373523	2
Caelo	Propyl-4-hydroxybenzoate	13365009	3

- 111 085 spectra from 742 *Apo-Ident* customers from a total of 31 837 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Propyl-4-hydroxybenzoate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Propyl-4-hydroxybenzoate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	40	0	119 102
Type C	0	150	12	111 085

The substance/substance group *Propyl-4-hydroxybenzoate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	92.5926 % (> 90.7407 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Propyl-4-hydroxybenzoate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chlorocresol	27.73	—
Serine	28.42	—
Sodium cromoglicate	29.53	—
Levothyroxin sodium	35.89	—
Choline hydrogen tartrate	39.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Propyl-4-hydroxybenzoate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20981	20981	0.00	28.41
21758	22754	7.78	26.73
22754	22754	0.00	28.37
22765	22765	0.00	27.86
24497	24497	0.00	29.46

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Propyphenazone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20805-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Propyphenazone; Propyphenazonum

Special notes

When selecting the *Propyphenazone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Propyphenazone	4	3	29

Second-stage model

For differentiation of the substance/substance group *Propyphenazone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Propyphenazone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Propyphenazone	12039103	20805	40	1402051
Caelo	Propyphenazone	13332206	21454	60	20131009
Fagron	Propyphenazone	16E02-B08-327928	23261	40	20160602
Fagron	Propyphenazone	16H25-B01-334972	23922	40	20161227

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Propyphenazone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Propyphenazone*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Propyphenazone	15348908	23254	40
Caelo	Propyphenazone	172776	23861	40
Caelo	Propyphenazone	190190	24528	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 56 spectra from 18 *Apo-Ident* customers from 33 batches from the substance/substance group *Propyphenazone*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Propyphenazone	12039112	1
Caelo	Propyphenazone	13332205	3
Caelo	Propyphenazone	13137104	1
Caelo	Propyphenazone	15122502	1
Caelo	Propyphenazone	15122505	1
Caelo	Propyphenazone	15348902	2
Caelo	Propyphenazone	15348904	2
Caelo	Propyphenazone	15348908	2
Caelo	Propyphenazone	15348914	2
Caelo	Propyphenazone	15348910	1
Caelo	Propyphenazone	17351302	1
Caelo	Propyphenazone	15348901	1
Caelo	Propyphenazone	12039101	2
Caelo	Propyphenazone	15348913	4
Caelo	Propyphenazone	15348912	2
Caelo	Propyphenazone	17351305	1
Caelo	Propyphenazone	13036702	2
Fagron	Propyphenazone	13B12-B02-297171	1
Fagron	Propyphenazone	13K20-B03-302291	1
Fagron	Propyphenazone	17G03-B01-347588	2
Fagron	Propyphenazone	13K20-B03	2
Fagron	Propyphenazone	13K-B03-319137	1
Fagron	Propyphenazone	13k20-b03-319137	1
Fargon	Propyphenazone	11H31-N07	1
Gatt-Koller	Propyphenazone	1800011	1
Gatt-Koller / Phoenix	Propyphenazone	419/02123112	1
Fagron	Propyphenazone	13K20-B03-319137	3
Fagron	Propyphenazone	13K20-B03-311715	3
Fagron	Propyphenazone	13K20B03319137	1
Nachprüfung vom 31.02.2...	Propyphenazone	13B12-B02-297171	1
Raben-Apotheke Mildenau	Propyphenazone	12039103	1
Caelo	Propyphenazone	15122504	3
Caelo	Propyphenazone	12039103	1
Euro OTC	Propyphenazone		1
Fagron	Propyphenazone	16E02-B08-327928	2

- 111 191 spectra from 742 *Apo-Ident* customers from a total of 31 858 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Propyphenazone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Propyphenazone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	120	0	119 022
Type C	0	55	1	111 191

The substance/substance group *Propyphenazone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	98.2143 % (> 92.8571 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Propyphenazone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ethyl hydrogen fumarate calcium	28.15	—
Cyproterone acetate	39.43	—
Griseofulvin	41.97	—
Omeprazole	43.37	—
Prilocaine hydrochloride	50.97	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Propyphenazone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20805	20805	0.00	41.11
21454	20805	3.94	40.87
23261	20805	6.82	41.17
23922	20805	10.36	41.93

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Pyridoxal-5-phosphate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20830-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pyridoxal-5-phosphate; Pyridoxali phosphas

Special notes

When selecting the *Pyridoxal-5-phosphate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pyridoxal-5-phosphate	7	2	8

Second-stage model

For differentiation of the substance/substance group *Pyridoxal-5-phosphate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pyridoxal-5-phosphate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Pyridoxal-5-phos...	1302029-01	20830	40	8897
Euro OTC	Pyridoxal-5-phos...	1302029-01	21097	40	20130315
Euro OTC	Pyridoxal-5-phos...	1701015	23133	40	20170220*
Euro OTC	Pyridoxal-5-phos...	1701015-01	23276	40	20170220
Euro OTC	Pyridoxal-5-phos...	1808030	24329	40	20181019*
Euro OTC	Pyridoxal-5-phos...	1902022	24542	40	20190320*
Euro OTC	Pyridoxal-5-phos...	1908001	24833	40	20190903*
Euro OTC	Pyridoxal-5-phos...	1910027	24923	40	20191217*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 8 reference samples from the substance/substance group *Pyridoxal-5-phosphate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 369 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Pyridoxal-5-phosphate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Pyridoxal-5-phosphate	1711030	23877	40
Euro OTC	Pyridoxal-5-phosphate	2001043	25130	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 13 spectra from 8 *Apo-Ident* customers from 10 batches from the substance/substance group *Pyridoxal-5-phosphate*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Denk	Pyridoxal-5-phosphate	C041402802	1
Denk	Pyridoxal-5-phosphate	20171202	1
Euro OTC	Pyridoxal-5-phosphate	1808030-01	1
Euro OTC	Pyridoxal-5-phosphate	1902022-01	1
Euro OTC	Pyridoxal-5-phosphate	1908001-01	1
Euro OTC	Pyridoxal-5-phosphate	1711030-01	2
Euro OTC	Pyridoxal-5-phosphate	1808030-02	1
Inresa Arznei	Pyridoxal-5-phosphate	13100411	1
Euro OTC	Pyridoxal-5-phosphate	1701015-01	3
Euro OTC	Pyridoxal-5-phosphate	1808030	1

- 111 234 spectra from 742 *Apo-Ident* customers from a total of 31 881 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pyridoxal-5-phosphate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pyridoxal-5-phosphate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	80	0	119 062
Type C	0	13	0	111 234

The substance/substance group *Pyridoxal-5-phosphate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pyridoxal-5-phosphate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carbomers 35000 / 50000	28.75	—
Ascorbic acid	47.52	—
Magnesium citrate	56.98	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pyridoxal-5-phosphate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24542	24542	0.00	67.05
24833	24833	0.00	66.86
24923	24923	0.00	60.34
24329	24329	0.00	57.11
20830	20830	0.00	50.46
21097	20830	3.37	48.29
23133	23133	0.00	48.64
23276	20830	4.45	54.73

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Pyridoxine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20440-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Pyridoxine hydrochloride; Pyridoxini hydrochloridum

Special notes

When selecting the *Pyridoxine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Pyridoxine hydrochloride	6	6	35

Second-stage model

For differentiation of the substance/substance group *Pyridoxine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Pyridoxine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Pyridoxine hydro...	14262302	21675	60	20141002
Caelo	Pyridoxine hydro...	162225	22770	40	20160825*
Euro OTC	Pyridoxine hydro...	1401044-01	21678	60	20140221
Euro OTC	Pyridoxine hydro...	1407009-01	21773	60	20140807
Euro OTC	Pyridoxine hydro...	1507012	21846	60	20150721*
Euro OTC	Pyridoxine hydro...	1601039	22300	60	20160203*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 6 reference samples from the substance/substance group *Pyridoxine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 349 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Pyridoxine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Pyridoxine hydrochloride	180287	24024	40
Euro OTC	Pyridoxine hydrochloride	1604063	22569	40
Euro OTC	Pyridoxine hydrochloride	1608035	22798	40
Euro OTC	Pyridoxine hydrochloride	1710014	23735	40
Euro OTC	Pyridoxine hydrochloride	1806022-01	24189	40
Euro OTC	Pyridoxine hydrochloride	1908009	24838	40

- 118902 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 76 spectra from 16 *Apo-Ident* customers from 36 batches from the substance/substance group *Pyridoxine hydrochloride*.
- Among them are spectra of independent samples from 35 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Pyridoxine hydrochloride	11021406	1
Caelo	Pyridoxine hydrochloride	13102509	2
Caelo	Pyridoxine hydrochloride	13102516	1
Caelo	Pyridoxine hydrochloride	15218707	1
Caelo	Pyridoxine hydrochloride	15218713	3
Caelo	Pyridoxine hydrochloride	15218709	1
Caelo	Pyridoxine hydrochloride	16222514	2
Caelo	Pyridoxine hydrochloride	16222504	1
Caelo	Pyridoxine hydrochloride	16222521	1
Caelo	Pyridoxine hydrochloride	16222506	2
Caelo	Pyridoxine hydrochloride	16222515	2
Caelo	Pyridoxine hydrochloride	18028703	1
Caelo	Pyridoxine hydrochloride	13102510	2
Caelo	Pyridoxine hydrochloride	16222501	5
Caelo	Pyridoxine hydrochloride	12214119	2
Caelo	Pyridoxine hydrochloride	14262306	1
Caelo	Pyridoxine hydrochloride	15218702	6
Caelo	Pyridoxine hydrochloride	11197009	1
Caelo	Pyridoxine hydrochloride	12214102	2
Caelo	Pyridoxine hydrochloride	12102510	1
Caelo	Pyridoxine hydrochloride	16222520	1
Caesar & Loretz GmbH D-...	Pyridoxine hydrochloride	11197009	5
Caesar & Loretz GmbH, 4...	Pyridoxine hydrochloride	12214102	5
Caesar & Loretz GmbH, 4...	Pyridoxine hydrochloride	12214110	2
Caesar & Loretz GmbH, 4...	Pyridoxine hydrochloride	12214115	7
Caesar & Loretz GmbH, 4...	Pyridoxine hydrochloride	12214119	2
Euro OTC	Pyridoxine hydrochloride	160803501	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Pyridoxine hydrochloride	1710014-01	1
Euro OTC	Pyridoxine hydrochloride	17001401	1
Euro OTC	Pyridoxine hydrochloride	1601039-01	1
Euro OTC	Pyridoxine hydrochloride	1110001-01	1
Euro OTC	Pyridoxine hydrochloride	1206022-02	1
Euro OTC	Pyridoxine hydrochloride	1604063-01	1
Fagron	Pyridoxine hydrochloride	1608035-01	1
Fagron	Pyridoxine hydrochloride	L13080030	1
Fagron	Pyridoxine hydrochloride	12e02-n02	1
Farmalabor	Pyridoxine hydrochloride	P1701531-000	1
Caelo	Pyridoxine hydrochloride	15218710	2
Caelo	Pyridoxine hydrochloride	14262302	3

- 111 171 spectra from 742 *Apo-Ident* customers from a total of 31 855 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Pyridoxine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Pyridoxine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	240	0	118 902
Type C	0	75	1	111 171

The substance/substance group *Pyridoxine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 99.8899 %)	98.6842 % (> 94.7368 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Pyridoxine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium ascorbate	58.90	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Pyridoxine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21675	21846	6.32	68.96
21678	21846	6.39	68.90
21773	21846	0.94	69.65
21846	21846	0.00	69.42
22300	22300	0.00	69.57
22770	22770	0.00	69.49

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Quinidine sulfate dihydrate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20819-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Quinidine sulfate dihydrate; Chinidini sulfas; Quinidine sulfate

Special notes

When selecting the *Quinidine sulfate dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinidine sulfate dihydrate	3	2	3

Second-stage model

For differentiation of the substance/substance group *Quinidine sulfate dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinidine sulfate dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Quinidine sulfat...	12L04-N10	20819	40	AR-14-FG-013249-01
Fagron	Quinidine sulfat...	12J16-B03	21217	39	1412323
Fagron	Quinidine sulfat...	14I04-B09-304357	21810	60	AR-15-FG-015409-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 139 spectra of 3 reference samples from the substance/substance group *Quinidine sulfate dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 550 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Quinidine sulfate dihydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Quinidine sulfate dihydrate	16A06-B04-324954	22970	40
Fagron	Quinidine sulfate dihydrate	18B01-B08-350965	24181	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Quinidine sulfate dihydrate*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
buchler GmbH	Quinidine sulfate dihydrate	16a06-b04-340797	1
Fagron	Quinidine sulfate dihydrate	13G08-N02	1
Fagron	Quinidine sulfate dihydrate	18B01-B08-356315	1

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinidine sulfate dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinidine sulfate dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	139	0	110 550
Type B	0	80	0	119 062
Type C	0	3	0	111 244

The substance/substance group *Quinidine sulfate dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.6835 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinidine sulfate dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinine sulfate	46.15	—
Dequalinium chloride	52.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinidine sulfate dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20819	20819	0.00	48.61
21217	21217	0.00	46.97
21810	21810	0.00	46.15

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Quinine dihydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 23186-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Quinine dihydrochloride; Chinini dihydrochloridum

Special notes

When selecting the *Quinine dihydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinine dihydrochloride	2	2	0

Second-stage model

For differentiation of the substance/substance group *Quinine dihydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinine dihydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Quinine dihydroc...	172129	23636	40	20173008*
Caelo	Quinine dihydroc...	172072	23655	40	20170830*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 80 spectra of 2 reference samples from the substance/substance group *Quinine dihydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 609 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Quinine dihydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Quinine dihydrochloride	16269603	23185	40
Caelo	Quinine dihydrochloride	162696	23358	40
Caelo	Quinine dihydrochloride	16269603	23186	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Quinine dihydrochloride*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinine dihydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinine dihydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	80	0	110 609
Type B	0	120	0	119 022
Type C	0	0	0	111 247

The substance/substance group *Quinine dihydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinine dihydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	48.56	—
Sulfogaiacol hydrate	58.60	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinine dihydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23636	23636	0.00	71.15
23655	23655	0.00	70.41

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Quinine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20547-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Quinine hydrochloride; Chinini hydrochloridum

Special notes

When selecting the *Quinine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinine hydrochloride	4	3	9

Second-stage model

For differentiation of the substance/substance group *Quinine hydrochloride* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Quinine hydrochl...	15376201	22309	60	20151105
Caelo	Quinine hydrochl...	16283302	23577	40	1802260
Fagron	Quinine hydrochl...	13G10-N07	21235	30	20130809
Fagron	Quinine hydrochl...	13I30-B02-295630	21809	60	AR-15-FG-015410-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 190 spectra of 4 reference samples from the substance/substance group *Quinine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 499 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Quinine hydrochloride*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Quinine hydrochloride	180226	24022	40
Fagron	Quinine hydrochloride	15A20-B03-319027	23573	40
Fagron	Quinine hydrochloride	16K01-B05-340171	23920	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 11 *Apo-Ident* customers from 11 batches from the substance/substance group *Quinine hydrochloride*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Quinine hydrochloride	18022604	1
Caelo	Quinine hydrochloride	12316604	1
Caelo	Quinine hydrochloride	16283305	1
Caelo	Quinine hydrochloride	12316605	1
Caelo	Quinine hydrochloride	13D24-N06	1
Fagron	Quinine hydrochloride	10N129B	1
Gatt-Koller	Quinine hydrochloride	3500/08103810	1
Caelo	Quinine hydrochloride	12316611	1
Caelo	Quinine hydrochloride	153776201	1
Caelo	Quinine hydrochloride	16283302	1
Fagron	Quinine hydrochloride	13G10-N07	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 880 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	190	0	110 499
Type B	0	120	0	119 022
Type C	0	11	0	111 236

The substance/substance group *Quinine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.8421 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinine sulfate	16.36	77.13
Sodium cromoglicate	50.99	—
⋮	⋮	⋮
Estriol	>50	124.97
Progesterone, micronized	>50	389.67
Alfatradiol	>50	408.95
Spironolactone	>50	438.93
Pregnenolone	>50	452.99
Testosterone propionate	>50	599.37

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21809	21809	0.00	18.62
22309	23577	1.37	16.39
21235	23577	5.35	19.97
23577	23577	0.00	16.36

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Quinine sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21057-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Quinine sulfate; Chinini sulfas

Special notes

When selecting the *Quinine sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinine sulfate	4	2	6

Second-stage model

For differentiation of the substance/substance group *Quinine sulfate* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinine sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Quinine sulfate	13024604	21429	60	AR-16-FG-005472-01
Caelo	Quinine sulfate	15230005	22959	40	20150729
Fagron	Quinine sulfate	13J23-N03	21057	40	1404401
Fagron	Quinine sulfate	14B27-B01	21277	40	AR-16-FG-009455-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 4 reference samples from the substance/substance group *Quinine sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 509 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Quinine sulfate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Quinine sulfate	170616	23281	40
Caelo	Quinine sulfate	180630	24032	40
Caelo	Quinine sulfate	170616	23316	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 9 spectra from 3 *Apo-Ident* customers from 6 batches from the substance/substance group *Quinine sulfate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Quinine sulfate	15B06B03304359	1
Gatt-Koller	Quinine sulfate	1803149	4
Gatt-Koller	Quinine sulfate	1801042	1
Gatt-Koller / Phoenix	Quinine sulfate	4928/11132214	1
Gatt-Koller / Phoenix	Quinine sulfate	2503/07143314	1
KÖGL	Quinine sulfate	1901102	1

- 111 238 spectra from 742 *Apo-Ident* customers from a total of 31 885 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinine sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinine sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	180	0	110 509
Type B	0	120	0	119 022
Type C	0	9	0	111 238

The substance/substance group *Quinine sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinine sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinine hydrochloride	18.02	69.42
Quinidine sulfate dihydrate	49.99	—
Sodium cromoglicate	50.21	—
⋮	⋮	⋮
Estriol	>50	134.61
Alfatradiol	>50	342.47
Progesterone, micronized	>50	370.10
Spironolactone	>50	415.56
Pregnenolone	>50	485.40
Testosterone propionate	>50	509.48

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinine sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21057	21057	0.00	18.42
21277	21277	0.00	18.02
21429	21429	0.00	20.14
22959	21429	3.89	20.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Quinoline yellow**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20456-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Quinoline yellow

Special notes

When selecting the *Quinoline yellow* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinoline yellow	4	3	42

Second-stage model

For differentiation of the substance/substance group *Quinoline yellow* the following second-stage model is used:

- [Submodel 8](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinoline yellow*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Quinoline yellow	12042010	20922	40	20120314
Caelo	Quinoline yellow	13109108	21305	40	1711481
Caelo	Quinoline yellow	17034101	23400	40	1709327
Caelo	Quinoline yellow	172277	24812	40	20171020*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Quinoline yellow*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 210 spectra of 5 reference samples from the substance/substance group *Quinoline yellow*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Quinoline yellow	16050101	23401	40
Caelo	Quinoline yellow	190734	24555	40
Fagron	Quinoline yellow	12E24-N01	20731	60
Caelo	Quinoline yellow	172277	23685	30
Caelo	Quinoline yellow	190734	24725	40

- 118932 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 93 spectra from 54 *Apo-Ident* customers from 44 batches from the substance/substance group *Quinoline yellow*.
- Among them are spectra of independent samples from 42 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Quinoline yellow	17227709	2
Caelo	Quinoline yellow	11089606	1
Caelo	Quinoline yellow	20301211-6	1
Caelo	Quinoline yellow	713E-03146	1
Caelo	Quinoline yellow	12042002	3
Caelo	Quinoline yellow	11089608	1
Caelo	Quinoline yellow	12042004	1
Caelo	Quinoline yellow	14363207	1
Caelo	Quinoline yellow	15276802	1
Caelo	Quinoline yellow	15276801	2
Caelo	Quinoline yellow	16050101	5
Caelo	Quinoline yellow	17034104	6
Caelo	Quinoline yellow	118E-03146	1
Caelo	Quinoline yellow	17227701	5
Caelo	Quinoline yellow	12051810	1
Caelo	Quinoline yellow	17227703	4
Caelo	Quinoline yellow	17227702	1
Caelo	Quinoline yellow	17227706	5
Caelo	Quinoline yellow	17227705	1
Caelo	Quinoline yellow	14274305	1
Caelo	Quinoline yellow	16050106	3
Caelo	Quinoline yellow	11089610	1
Caelo	Quinoline yellow	14363202	4
Caelo	Quinoline yellow	19073401	6
Caelo	Quinoline yellow	12042007	3
Caelo	Quinoline yellow	13109109	1
Caelo	Quinoline yellow	15276803	2
Caelo	Quinoline yellow	15276804	2
Caelo	Quinoline yellow	16050108	1
Caelo	Quinoline yellow	13109102	2
Caelo	Quinoline yellow	14274309	1
Caelo	Quinoline yellow	14049401	2
Caelo	Quinoline yellow	17034102	5

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Quinoline yellow	17227705	1
Fagron	Quinoline yellow	9878	1
Fagron	Quinoline yellow	12B08-N08	1
Fagron	Quinoline yellow	11F30-N04	1
Fagron	Quinoline yellow	11K08-N01	2
Fagron	Quinoline yellow	12E24-N05	1
Fagron	Quinoline yellow	14D18-B02-295783	1
Fagron	Quinoline yellow	12L11-N07	1
Fagron	Quinoline yellow	100427	1
Klosterring	Quinoline yellow	17227706	1
PHOENIX	Quinoline yellow	12042004	1
phönix	Quinoline yellow	15276803	1
sanacorp	Quinoline yellow	3214M-03146	1
Caelo	Quinoline yellow	12042010	1
Caelo	Quinoline yellow	17034101	1

- 111 154 spectra from 742 *Apo-Ident* customers from a total of 31 847 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinoline yellow* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinoline yellow* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	190	20	118 932
Type C	0	53	40	111 154

The substance/substance group *Quinoline yellow* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	90.4762 % (> 89.0476 %)
Type C	100.0000 % (> 99.8899 %)	56.9892 % (> 53.7634 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinoline yellow* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Midazolam hydrochloride	53.81	—
⋮	⋮	⋮
Saccharin sodium	53.90	67.60
Eosin Y	>50	102.37

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinoline yellow* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20922	21305	8.43	92.52
21305	21305	0.00	89.91
23400	23400	0.00	63.04
24812	24812	0.00	89.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Quinolinol sulfate potassium sulfate
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20573-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Quinolinol sulfate potassium sulfate; Chinolini et kalii sulfas; Quinolinol sulphate potassium sulphate

Special notes

When selecting the *Quinolinol sulfate potassium sulfate* substance/substance group, the following information is displayed to the user:

- Advice for the distinction from 8-hydroxyquinoline sulfate: 8-hydroxyquinoline sulfate is a spectrally similar substance, which is however currently not deliverable in Germany. Please decide, if an additional prove seems to be useful.

Applicable documents

978-3-7692-6679-5	<i>European Pharmacopoeia 9th Edition, Basic Version 2017</i> [3]
Komm2.2.40	<i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]
AA004	<i>Erstellung und Validierung eines IdentModul-Updates</i>

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Quinolinol sulfate potassium sulfate	4	1	20

Second-stage model

For differentiation of the substance/substance group *Quinolinol sulfate potassium sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Quinolinol sulfate potassium sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Quinolinol sulfa...	13071104	20983	40	1403095
Caelo	Quinolinol sulfa...	13403501	21430	60	20131218
Caelo	Quinolinol sulfa...	15147704	22606	40	20150618
Caelo	Quinolinol sulfa...	15147704	22607	40	20150618
Caelo	Quinolinol sulfa...	162218	22626	40	20160808*

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Quinolinol sulfate potassium sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110469 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Quinolinol sulfate potassium sulfate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Quinolinol sulfate potassium...	16221809	23563	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 202 spectra from 109 *Apo-Ident* customers from 23 batches from the substance/substance group *Quinolinol sulfate potassium sulfate*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
29.04.15 Spangro	Quinolinol sulfate potassium...	140804	1
apomix	Quinolinol sulfate potassium...	16221809	1
Bomb/Gehe	Quinolinol sulfate potassium...	140804	1
Bombastus	Quinolinol sulfate potassium...	140804	3
Caelo	Quinolinol sulfate potassium...	7051305	1
Caelo	Quinolinol sulfate potassium...	15147701	3
Caelo	Quinolinol sulfate potassium...	15147714	1
Caelo	Quinolinol sulfate potassium...	16221804	1
Caelo	Quinolinol sulfate potassium...	13403506	12
Caelo	Quinolinol sulfate potassium...	13071101	2
Caelo	Quinolinol sulfate potassium...	140804	4
Caelo	Quinolinol sulfate potassium...	15147706	4
Caelo	Quinolinol sulfate potassium...	120905	1
Caelo	Quinolinol sulfate potassium...	10281601	1
Caelo	Quinolinol sulfate potassium...	13071106	1
Caelo	Quinolinol sulfate potassium...	15147708	4
Caelo	Quinolinol sulfate potassium...	16221809	4
Caelo	Quinolinol sulfate potassium...	9106304	1
Caelo	Quinolinol sulfate potassium...	13403513	1
Caelo	Quinolinol sulfate potassium...	16221807	2
Caelo	Quinolinol sulfate potassium...	16221811	1
Caesar & Loretz GmbH / ...	Quinolinol sulfate potassium...	16221807	1
Dermapharm	Quinolinol sulfate potassium...	100804	11
Dermapharm	Quinolinol sulfate potassium...	140804	1
Dermapharm	Quinolinol sulfate potassium...	140804	53
Dermapharm	Quinolinol sulfate potassium...	120905	43
Dermapharm	Quinolinol sulfate potassium...	1470804	1
Dermapharm AG/Noweda	Quinolinol sulfate potassium...	140804	1
dermopharm/Noweda	Quinolinol sulfate potassium...	120905	1
Ebert-Jacobi	Quinolinol sulfate potassium...	16221804	1
Euro OTC	Quinolinol sulfate potassium...	140804	3
Fagron	Quinolinol sulfate potassium...	140804	3
GEHE	Quinolinol sulfate potassium...	15147706	1
Geilenkirchen/Dermopham	Quinolinol sulfate potassium...	140804	1
Mibe	Quinolinol sulfate potassium...	120905	1
Mibe/Gehe	Quinolinol sulfate potassium...	140804	1
Nachprüfung	Quinolinol sulfate potassium...	2812U03423	1

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Supplier	Substance	Batch	Spectra
Nachprüfung	Quinolinol sulfate potassium...	13071104	1
Nachprüfung	Quinolinol sulfate potassium...	120905	1
Noweda	Quinolinol sulfate potassium...	140804	1
Pharmachen	Quinolinol sulfate potassium...	140804	1
phönix	Quinolinol sulfate potassium...	140804	1
Phönix Gotha	Quinolinol sulfate potassium...	120905	4
Phönix Gotha	Quinolinol sulfate potassium...	140804	1
sanacorp	Quinolinol sulfate potassium...	120905	1
siehe Protokoll	Quinolinol sulfate potassium...	140804	1
Stumpf	Quinolinol sulfate potassium...	100804	1
Caelo	Quinolinol sulfate potassium...	13071104	4
Caelo	Quinolinol sulfate potassium...	13403501	7
Caelo	Quinolinol sulfate potassium...	15147704	4

- 111 045 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Quinolinol sulfate potassium - sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Quinolinol sulfate potassium sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	40	0	119 064
Type C	0	130	72	111 032

The substance/substance group *Quinolinol sulfate potassium sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8898 %)	64.3564 % (> 62.8713 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Quinolinol sulfate potassium sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their

Mahalanobis distance is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Eosin Y	63.86	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Quinolinol sulfate potassium sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22606	22626	2.69	86.07
22607	22626	2.56	86.27
22626	22626	0.00	86.36
21430	22626	11.61	85.03
20983	20983	0.00	77.09

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Resocrinol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20938-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Resocrinol; Resorcinolum

Special notes

When selecting the *Resocrinol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Resocrinol	4	1	69

Second-stage model

For differentiation of the substance/substance group *Resocrinol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Resocrinol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Resocrinol	13293108	21471	60	AR-15-FG-006906-01
Caelo	Resocrinol	161533	22632	40	20160524*
Fagron	Resocrinol	12G24-N04	20938	40	1401462
Fagron	Resocrinol	13I18-B09-291533	21706	45	20130606

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 185 spectra of 4 reference samples from the substance/substance group *Resocrinol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 504 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Resocrinol*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Resocrinol	17H03-B11-338899	23921	40

- 119102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 153 spectra from 105 *Apo-Ident* customers from 72 batches from the substance/substance group *Resocrinol*.
- Among them are spectra of independent samples from 69 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Resocrinol	14G10-B06-296297	2
Caelo	Resocrinol	18216601	1
Caelo	Resocrinol	10111210	1
Caelo	Resocrinol	11309610	4
Caelo	Resocrinol	5052	1
Caelo	Resocrinol	19061305	1
Caelo	Resocrinol	12255614	2
Caelo	Resocrinol	15009502	1
Caelo	Resocrinol	2041512	1
Caelo	Resocrinol	13293115	2
Caelo	Resocrinol	15009515	2
Caelo	Resocrinol	16153306	1
Caelo	Resocrinol	18111703	1
Caelo	Resocrinol	18130901	1
Caelo	Resocrinol	18216603	2
Caelo	Resocrinol	15K24-B02-317584	1
Caelo	Resocrinol	10218809	2
Caelo	Resocrinol	16153307	1
Caelo	Resocrinol	12G24-N04	2
Caelo	Resocrinol	13/18-B19-291534	1
Caelo	Resocrinol	206370-0003	1
Caelo	Resocrinol	16153313	2
Caelo	Resocrinol	15009507	7
Caelo	Resocrinol	16153312	1
Caelo	Resocrinol	18216611	1
Caelo	Resocrinol	16153309	7
Caelo	Resocrinol	18015601	1
Caelo	Resocrinol	18216609	1
Caelo	Resocrinol	16D29-B01	1
Caelo	Resocrinol	16271807	1
Caelo	Resocrinol	13293103	1
Caesar & Loretz GmbH / ...	Resocrinol	18216603	1
Euro OTC	Resocrinol	11/13-N02	1
Fagron	Resocrinol	11A19-N09	1
Fagron	Resocrinol	2112I-02170	1
Fagron	Resocrinol	12K30-N03	4
Fagron	Resocrinol	12g24-N04	1

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Supplier	Substance	Batch	Spectra
Fagron	Resocrinol	11/13-N02	2
Fagron	Resocrinol	1112013A	1
Fagron	Resocrinol	14/16062	1
Fagron	Resocrinol	118b09291534	1
Fagron	Resocrinol	14G10B06	1
Fagron	Resocrinol	13I18-B09-291534	1
Fagron	Resocrinol	14J15-B02-307749	5
Fagron	Resocrinol	14J15-B02	1
Fagron	Resocrinol	15K24-B02-317584	2
Fagron	Resocrinol	16D29-B01-329760	3
Fagron	Resocrinol	16D29-B01-332738	2
Fagron	Resocrinol	17H03-B11-338899	1
Fagron	Resocrinol	17H03-B11-342399	1
Fagron	Resocrinol	18K20-B01-355679	1
Fagron	Resocrinol	16d29b01323046	1
Fagron	Resocrinol	16d29b01332738	1
Fagron	Resocrinol	16D29-B01-323046	2
Fagron	Resocrinol	11L19-N19	2
Fagron	Resocrinol	18B08-B05-347787	4
Fagron	Resocrinol	13I18-B09	2
Fagron	Resocrinol	10B01-N06	2
Fagron	Resocrinol	13/18-B09-291534	1
Fagron	Resocrinol	14/19050	1
Fagron	Resocrinol	14G10-B06-296296	7
Fagron	Resocrinol	12G24-N004	1
Fagron	Resocrinol	13E24-N10	8
Fagron	Resocrinol	13/17071	1
Fagron	Resocrinol	16D29-B01	1
Fargon	Resocrinol	15K24-B02-317584	1
Gehe	Resocrinol	11L13-N02	1
Gehe	Resocrinol	13E24-N10	1
L12	Resocrinol	16153306	1
Caelo	Resocrinol	15009511	4
Noweda	Resocrinol	13E24-N10	1
Noweda	Resocrinol	1318b09291533	1
Noweda	Resocrinol	14G10-B06-296	1
Noweda/Fargon	Resocrinol	16029-B01-329760	1
Phoenix WE: 13.07.2015	Resocrinol	14G10-B06-296296	1
Phoenix goettin	Resocrinol	13I18-B09-291534	1
Phönix Gotha	Resocrinol	14G10-B06-296296	1
Fagron	Resocrinol	15/18082	1
Sanacorp	Resocrinol	16D29-B01-323046	1
Caelo	Resocrinol	11d29-n14	2
Caelo	Resocrinol	13293110	1
Fagron	Resocrinol	11/13-no2	1
vdl	Resocrinol	12G24-N04	1
Fagron	Resocrinol	12G24-N04	10
Fagron	Resocrinol	13I18-B09-291533	1

- 111 094 spectra from 742 *Apo-Ident* customers from a total of 31 820 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Resocrinol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Resocrinol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	185	0	110 504
Type B	0	40	0	119 102
Type C	0	144	9	111 094

The substance/substance group *Resocrinol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.7568 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	94.1176 % (> 92.1569 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Resocrinol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hydroquinone	23.00	—
Sodium cromoglicate	30.34	—
Levothyroxin sodium	47.63	—
Serine	55.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Resocrinol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21706	21471	4.47	25.18
20938	20938	0.00	31.96
21471	21471	0.00	28.92
22632	22632	0.00	28.30

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ribavirin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22346-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ribavirin; Ribavirinum

Special notes

When selecting the *Ribavirin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ribavirin	2	2	0

Second-stage model

For differentiation of the substance/substance group *Ribavirin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ribavirin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Ribavirin	1308001	22382	45	20130902*
Euro OTC	Ribavirin	1604012	22528	40	20160428*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 85 spectra of 2 reference samples from the substance/substance group *Ribavirin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 604 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 85 spectra of 2 reference samples from the substance/substance group *Ribavirin*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Ribavirin	1304027-01	22346	45
Euro OTC	Ribavirin	1304027-02	23023	40

- 119057 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Ribavirin*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ribavirin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ribavirin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	85	0	110 604
Type B	0	85	0	119 057
Type C	0	0	0	111 247

The substance/substance group *Ribavirin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 92.9412 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.9412 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ribavirin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	28.39	—
Xylitol	37.13	—
Potassium citrate	41.88	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ribavirin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22382	22382	0.00	28.01
22528	22528	0.00	28.22

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Riboflavin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20409-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Riboflavin; Riboflavinum

Special notes

When selecting the *Riboflavin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Riboflavin	9	7	30

Second-stage model

For differentiation of the substance/substance group *Riboflavin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Riboflavin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Riboflavin	12003317	20925	40	1405155
Caelo	Riboflavin	13305203	21389	60	AR-15-FG-005686-01
Caelo	Riboflavin	14322008	22492	40	AR-16-FG-013669-01
Euro OTC	Riboflavin	1701050	23004	40	20170214*
Euro OTC	Riboflavin	1701050-01	23091	40	20170214
Fagron	Riboflavin	13D02-N03	20825	40	AR-15-FG-000733-01
Fagron	Riboflavin	13D02-N03	20914	40	20130405
Fagron	Riboflavin	15G20-B13-310997	21955	60	20150819
Fagron	Riboflavin	16B18-B06-319026	22655	40	AR-16-FG-014466-01
Fagron	Riboflavin	17G14-B05-337885	23714	40	AR-18-FG-000141-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 10 reference samples from the substance/substance group *Riboflavin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 249 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 280 spectra of 7 reference samples from the substance/substance group *Riboflavin*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Riboflavin	15330708	23579	40
Caelo	Riboflavin	172722	23649	40
Caelo	Riboflavin	192609	24884	40
Euro OTC	Riboflavin	1707017	23612	40
Euro OTC	Riboflavin	1801018	23880	40
Euro OTC	Riboflavin	1809004	24297	40
Euro OTC	Riboflavin	1810005	24307	40

- 118862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 36 spectra from 23 *Apo-Ident* customers from 33 batches from the substance/substance group *Riboflavin*.
- Among them are spectra of independent samples from 30 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag/Anzag 11.09.18	Riboflavin	18B22-B01-347142	1
Caelo	Riboflavin	15330708	1
Caelo	Riboflavin	17272204	1
Caelo	Riboflavin	17G14-B05-337885	1
EuRho	Riboflavin	1810005-01	1
Euro OTC	Riboflavin	1701050-02	1
Euro OTC	Riboflavin	1707017-01	1
Euro OTC	Riboflavin	L1305039-01	1
Euro OTC	Riboflavin	L1210048-01	1
Fagron	Riboflavin	11K02-N01	1
Fagron	Riboflavin	13J29-B04-287534	1
Fagron	Riboflavin	14E01-B10-296718	1
Fagron	Riboflavin	16E18-B05-325274	1
Fagron	Riboflavin	1701050-01	1
Fagron	Riboflavin	16E-18-B05-325274	1
Fagron	Riboflavin	16I12-B05-329618	1
Fagron	Riboflavin	17H10-B06-340170	1
Fagron	Riboflavin	18822-B01-347142	2
Fagron	Riboflavin	18J10-B01-356142	1
Fagron	Riboflavin	18J10-B01-355004	1
Fagron	Riboflavin	167720-0005	1
Fagron	Riboflavin	16B18_b06_319026	1
Fagron	Riboflavin	14B03B07292071	1
Fagron	Riboflavin	13J29-B04-287533	1

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Supplier	Substance	Batch	Spectra
Fagron	Riboflavin	18D05-B04	1
Fagron	Riboflavin	18J10-B01	1
Fagron	Riboflavin	19F10-B07-191754	1
Fagron	Riboflavin	16J12-B05-329618	1
Gatt-Koller	Riboflavin	1803007	1
Noweda	Riboflavin	18J10-B01-355004	1
Fagron	Riboflavin	14K03-B04-304718	1
Fagron	Riboflavin	15I09-B02-315216	1
Vdl 09.05.14;Preis 7,45	Riboflavin	13305203/15R05	1
Fagron	Riboflavin	15G20-B13-310997	2

- 111 211 spectra from 742 *Apo-Ident* customers from a total of 31 858 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Riboflavin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Riboflavin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	110 249
Type B	0	280	0	118 862
Type C	0	35	1	111 211

The substance/substance group *Riboflavin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8899 %)	97.2222 % (> 88.8889 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Riboflavin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Polymyxin B sulfate	20.91	—
Magnesium citrate	22.32	—
Levothyroxin sodium	32.88	—
Riboflavin phosphate sodium	48.74	—
Bacitracin	49.43	—
Minoxidil	56.50	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Riboflavin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23714	23714	0.00	28.22
20914	20825	3.79	24.02
20825	20825	0.00	24.04
23091	23714	7.87	25.36
20925	20925	0.00	25.96
21389	21389	0.00	22.32
21955	21389	5.86	25.21
22492	22492	0.00	25.67
22655	22655	0.00	25.28
23004	23004	0.00	24.34

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Riboflavin phosphate sodium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20948-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Riboflavin phosphate sodium; Natrii lactoflavini phosphoricum

Special notes

When selecting the *Riboflavin phosphate sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Riboflavin phosphate sodium	3	2	0

Second-stage model

For differentiation of the substance/substance group *Riboflavin phosphate sodium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Riboflavin phosphate sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Riboflavin phosp...	13I26-N06	20948	40	1403705
Fagron	Riboflavin phosp...	15J02-B03-313137	22269	60	AR-16-FG-009883-02
Fagron	Riboflavin phosp...	17A03-B01-335897	23713	40	AR-18-FG-000920-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Riboflavin phosphate sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 85 spectra of 2 reference samples from the substance/substance group *Riboflavin phosphate sodium*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Riboflavin phosphate sodium	14J31-B07-300519	21707	45
Fagron	Riboflavin phosphate sodium	17H03-B13-347175	24113	40

- 119 057 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Riboflavin phosphate sodium*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Riboflavin phosphate sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Riboflavin phosphate sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	75	10	119 057
Type C	0	0	0	111 247

The substance/substance group *Riboflavin phosphate sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	88.2353 % (> 84.7059 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Riboflavin phosphate sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium citrate	13.64	—
Polymyxin B sulfate	41.88	—
Levothyroxin sodium	43.24	—
Calcium citrate tetrahydrate	44.56	—
Ambroxol hydrochloride	51.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Riboflavin phosphate sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23713	23713	0.00	16.35
20948	20948	0.00	13.64
22269	22269	0.00	16.37

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50% greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ropivacaine hydrochloride monohydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 10002307-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ropivacaine hydrochloride monohydrate; Ropivacaini hydrochloridum monohydricum

Special notes

When selecting the *Ropivacaine hydrochloride monohydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ropivacaine hydrochloride monohydrate	3	1	0

Second-stage model

For differentiation of the substance/substance group *Ropivacaine hydrochloride monohydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ropivacaine hydrochloride monohydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ropivacaine hydr...	181569	24871	40	20180802*
Euro OTC	Ropivacaine hydr...	1707006	23704	40	20171013*
Euro OTC	Ropivacaine hydr...	1903027	24607	40	20190416*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Ropivacaine hydrochloride monohydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Ropivacaine hydrochloride monohydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ropivacaine hydrochloride mo...	191139	24872	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Ropivacaine hydrochloride monohydrate*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ropivacaine hydrochloride monohydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ropivacaine hydrochloride monohydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	40	0	119 102
Type C	0	0	0	111 247

The substance/substance group *Ropivacaine hydrochloride monohydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ropivacaine hydrochloride monohydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dexamethasone	28.02	—
Dexamethasone acetate	40.92	—
Prednisolon dihydrogen phosphate dinat...	42.43	—
Lidocaine	47.35	—
Triamcinolone acetonide	48.31	—
Estradiol hemihydrate	49.36	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ropivacaine hydrochloride monohydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23704	23704	0.00	32.69
24607	24607	0.00	28.02
24871	24871	0.00	29.92

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Saccharin sodium**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20200-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Saccharin sodium; Saccharinum natricum; Sodium saccharin

Special notes

When selecting the *Saccharin sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Saccharin sodium	5	3	44

Second-stage model

For differentiation of the substance/substance group *Saccharin sodium* the following second-stage model is used:

- [Submodel 8](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Saccharin sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Saccharin sodium	172110	23643	40	20170831*
Caelo	Saccharin sodium	162210	23857	39	20160811*
Caelo	Saccharin sodium	172592	24409	40	20171206*
Fagron	Saccharin sodium	13I20-B06-291654	23020	40	AR-17-FG-012457-01
Fagron	Saccharin sodium	14F30-B02-296322	23452	40	AR-17-FG-022421-01
Fagron	Saccharin sodium	14F30-B02-296322	23453	40	AR-18-FG-007117-02

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 239 spectra of 6 reference samples from the substance/substance group *Saccharin sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 450 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Saccharin sodium*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Saccharin sodium	15087704	22769	40
Caelo	Saccharin sodium	182104	24381	40
Caelo	Saccharin sodium	190964	24499	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 163 spectra from 127 *Apo-Ident* customers from 46 batches from the substance/substance group *Saccharin sodium*.
- Among them are spectra of independent samples from 44 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
17270001	Saccharin sodium	17211002	1
Cael Sanacorp 05.02.2016	Saccharin sodium	15087703	1
Caeleo/ Krieger	Saccharin sodium	17329407	1
Caelo	Saccharin sodium	17329309	1
Caelo	Saccharin sodium	17329310	2
Caelo	Saccharin sodium	11172805	2
Caelo	Saccharin sodium	11172814	1
Caelo	Saccharin sodium	90542309	1
Caelo	Saccharin sodium	11025605	1
Caelo	Saccharin sodium	11025610	1
Caelo	Saccharin sodium	9381714	1
Caelo	Saccharin sodium	12139803	1
Caelo	Saccharin sodium	14029707	3
Caelo	Saccharin sodium	14029710	3
Caelo	Saccharin sodium	1402970	1
Caelo	Saccharin sodium	15087703	6
Caelo	Saccharin sodium	21092015A	1
Caelo	Saccharin sodium	15087713	15
Caelo	Saccharin sodium	14029709	1
Caelo	Saccharin sodium	16221005	13
Caelo	Saccharin sodium	16221010	1
Caelo	Saccharin sodium	17329405	4
Caelo	Saccharin sodium	8121801	1
Caelo	Saccharin sodium	17329409	5
Caelo	Saccharin sodium	12362607	3
Caelo	Saccharin sodium	16221009	3
Caelo	Saccharin sodium	14213402	3
Caelo	Saccharin sodium	13205411	1
Caelo	Saccharin sodium	17211001	2
Caelo	Saccharin sodium	14029705	6

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Supplier	Substance	Batch	Spectra
Caelo	Saccharin sodium	18210407	4
Caelo	Saccharin sodium	15084101	5
Caelo	Saccharin sodium	1236207	1
Caelo	Saccharin sodium	15087704	10
Caelo	Saccharin sodium	14213405	5
Caelo	Saccharin sodium	17211002	12
Caelo	Saccharin sodium	17329407	7
Caelo	Saccharin sodium	13205414	3
Caesar & Loretz GmbH	Saccharin sodium	17329311	1
Caesar & Loretz GmbH	Saccharin sodium	18210407	1
Caesar & Loretz GmbH / ...	Saccharin sodium	17329407	1
Caesar & Loretz GmbH Hi...	Saccharin sodium	13205418	2
Caesar&lorenz,Phoenix	Saccharin sodium	15084101	1
Cealo	Saccharin sodium	17329405	1
Cealo/ Noweda	Saccharin sodium	17329407	1
Euro OTC	Saccharin sodium	15087704	1
Euro OTC	Saccharin sodium	15087713	1
Fagron	Saccharin sodium	12K26-N09	1
Fagron	Saccharin sodium	12A13-N03	2
Fagron	Saccharin sodium	SH349/12	1
Fagron	Saccharin sodium	13D19-N01	1
Fargon	Saccharin sodium	12A13-N03	1
Gehe	Saccharin sodium	18210407	1
Ichthyol-Gesellschaft	Saccharin sodium	16221009	1
Jenne	Saccharin sodium	15087707	1
Kehr	Saccharin sodium	17329407	1
Nachprüfung von Novembe...	Saccharin sodium	14029707	2
Caelo	Saccharin sodium	19096403	1
Pharmachem	Saccharin sodium	17329407	1
Phoenix	Saccharin sodium	14F30-B02-296322	1
Phönix	Saccharin sodium	17329407	1
Sana 03.11.14 EK 3,95	Saccharin sodium	14029707	1
sanacorp	Saccharin sodium	13205418	1
Sanacorp	Saccharin sodium	17211002	1
Caelo	Saccharin sodium		1

- 111 084 spectra from 742 *Apo-Ident* customers from a total of 31 845 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Saccharin sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Saccharin sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	239	0	110 450
Type B	0	120	0	119 022
Type C	0	159	4	111 084

The substance/substance group *Saccharin sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.4895 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	97.5460 % (> 95.7055 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Saccharin sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinoline yellow	31.95	59.89
Sodium cromoglicate	58.13	—
⋮	⋮	⋮
Eosin Y	>50	82.17

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Saccharin sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23643	23643	0.00	93.09
23857	23857	0.00	93.80
24409	24409	0.00	89.03
23020	23020	0.00	36.57
23452	23452	0.00	49.53
23453	23453	0.00	39.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Salicylic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20015-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Salicylic acid; Acidum salicylicum

Special notes

When selecting the *Salicylic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Salicylic acid	7	10	372

Second-stage model

For differentiation of the substance/substance group *Salicylic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Salicylic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Salicylic acid	13344002	21436	60	20131029
Caelo	Salicylic acid	13344018	21760	60	20131020
Caelo	Salicylic acid	160109	22443	60	20160229*
Euro OTC	Salicylic acid	1110020-01	20696	40	20120125
Euro OTC	Salicylic acid	1509007	21906	60	20150929*
Fagron	Salicylic acid	16115-B08-333932	23592	40	20170210
Fagron	Salicylic acid	190263	24591	40	20190121

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 7 reference samples from the substance/substance group *Salicylic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 329 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 420 spectra of 10 reference samples from the substance/substance group *Salicylic acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Salicylic acid	160500	22448	60
Caelo	Salicylic acid	171333	23277	40
Caelo	Salicylic acid	173015	23827	40
Caelo	Salicylic acid	182300	24236	40
Caelo	Salicylic acid	192209	24883	40
Euro OTC	Salicylic acid	1605023	22685	40
Euro OTC	Salicylic acid	1707009	23556	40
Euro OTC	Salicylic acid	1801042	23968	40
Euro OTC	Salicylic acid	1901015	24471	40
Euro OTC	Salicylic acid	1910018	24925	40

- 118 722 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1981 spectra from 593 *Apo-Ident* customers from 388 batches from the substance/substance group *Salicylic acid*.
- Among them are spectra of independent samples from 371 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Salicylic acid	KNC0461J15	1
Caelo	Salicylic acid	170700902	1
Caelo	Salicylic acid	16050005	9
AHD	Salicylic acid	13344002	1
AHD 22.07.14	Salicylic acid	134002	1
Fagron	Salicylic acid	14E26-B04_294623	1
Fagron	Salicylic acid	190264	2
Alliance 19.12.12	Salicylic acid	11311906	1
Alliance Healthcare	Salicylic acid	12036215	2
Alliance Healthcare	Salicylic acid	12036216	1
Alliance Healthcare	Salicylic acid	15211808	1
Anzag	Salicylic acid	1303020-01	2
Anzag	Salicylic acid	16050014	1
Fagron	Salicylic acid	13B14-N01	17
Anzag/Anzag 11.09.18	Salicylic acid	18F05-B02-350586	1
Anzag/Henry Lamotte	Salicylic acid	1334018	1
apo ident	Salicylic acid	1605023-01	1
Bombastus	Salicylic acid	12323403	1
Bombastus	Salicylic acid	14L02-B02-303557	1
Bombastus	Salicylic acid	12036223	1
Bombastus	Salicylic acid	1605023-01	1
Bombastus	Salicylic acid	16050017	1
Bombastus	Salicylic acid	17301505	1

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Supplier	Substance	Batch	Spectra
Caelo	Salicylic acid	14336911	1
Caelo	Salicylic acid	16312001	1
Caelo	Salicylic acid	7466	1
Caelo	Salicylic acid	1738980	1
Caelo	Salicylic acid	12134702	12
Caelo	Salicylic acid	12036315	1
Caelo	Salicylic acid	13H01-N01	1
Caelo	Salicylic acid	10355916	1
Caelo	Salicylic acid	10291817	1
Caelo	Salicylic acid	11311902	2
Caelo	Salicylic acid	11197117	1
Caelo	Salicylic acid	11311906	2
Caelo	Salicylic acid	11311910	2
Caelo	Salicylic acid	10001612	1
Caelo	Salicylic acid	9220715	1
Caelo	Salicylic acid	20270312-2	1
Caelo	Salicylic acid	20151112-4	1
Caelo	Salicylic acid	12H10-N08	5
Caelo	Salicylic acid	1197106	1
Caelo	Salicylic acid	12036209	4
Caelo	Salicylic acid	12036210	3
Caelo	Salicylic acid	3111J01045	1
Caelo	Salicylic acid	12036208	1
Caelo	Salicylic acid	11311917	4
Caelo	Salicylic acid	12036211	3
Caelo	Salicylic acid	12036223	8
Caelo	Salicylic acid	12134707	6
Caelo	Salicylic acid	10355911	2
Caelo	Salicylic acid	25041304	1
Caelo	Salicylic acid	12036215	2
Caelo	Salicylic acid	12323402	2
Caelo	Salicylic acid	A-100513-1	1
Caelo	Salicylic acid	12036226	7
Caelo	Salicylic acid	12036225	4
Caelo	Salicylic acid	12323401	1
Caelo	Salicylic acid	12036216	5
Caelo	Salicylic acid	12374205	8
Caelo	Salicylic acid	9091301	1
Caelo	Salicylic acid	123134712	1
Caelo	Salicylic acid	12134712	4
Caelo	Salicylic acid	9112013A	1
Caelo	Salicylic acid	20111306	1
Caelo	Salicylic acid	12374207	5
Caelo	Salicylic acid	13H01-N04	2
Caelo	Salicylic acid	12374211	17
Caelo	Salicylic acid	13032014A	1
Caelo	Salicylic acid	12374213	11
Caelo	Salicylic acid	12374208	2
Caelo	Salicylic acid	14076201	1
Caelo	Salicylic acid	7071403	1
Caelo	Salicylic acid	16072014A	1
Caelo	Salicylic acid	133454002	1
Caelo	Salicylic acid	14076206	6
Caelo	Salicylic acid	14076204	10
Caelo	Salicylic acid	13344014	6
Caelo	Salicylic acid	10112014B	1
Caelo	Salicylic acid	14076211	1
Caelo	Salicylic acid	18121412	1
Caelo	Salicylic acid	14300802	6
Caelo	Salicylic acid	1430802	1

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Supplier	Substance	Batch	Spectra
Caelo	Salicylic acid	13344020	15
Caelo	Salicylic acid	14300806	1
Caelo	Salicylic acid	14300805	11
Caelo	Salicylic acid	15084401	3
Caelo	Salicylic acid	14300804	6
Caelo	Salicylic acid	23071510	1
Caelo	Salicylic acid	15084403	7
Caelo	Salicylic acid	15084404	3
Caelo	Salicylic acid	15217301	6
Caelo	Salicylic acid	14336907	23
Caelo	Salicylic acid	15217302	17
Caelo	Salicylic acid	14336905	13
Caelo	Salicylic acid	8715	1
Caelo	Salicylic acid	15211806	2
Caelo	Salicylic acid	15211810	8
Caelo	Salicylic acid	14336911	20
Caelo	Salicylic acid	151224/1	1
Caelo	Salicylic acid	14336912	8
Caelo	Salicylic acid	6/20151706	1
Caelo	Salicylic acid	4515E-01045	1
Caelo	Salicylic acid	1433620	1
Caelo	Salicylic acid	16010905	11
Caelo	Salicylic acid	14336921	1
Caelo	Salicylic acid	16050003	2
Caelo	Salicylic acid	14336920	23
Caelo	Salicylic acid	15081601	1
Caelo	Salicylic acid	16010904	12
Caelo	Salicylic acid	16010906	11
Caelo	Salicylic acid	16010901	3
Caelo	Salicylic acid	160405AS	1
Caelo	Salicylic acid	16050004	15
Caelo	Salicylic acid	16010908	2
Caelo	Salicylic acid	2882	1
Caelo	Salicylic acid	Validierungsmessung	1
Caelo	Salicylic acid	16050011	11
Caelo	Salicylic acid	15211803	1
Caelo	Salicylic acid	16050012	12
Caelo	Salicylic acid	16010921	1
Caelo	Salicylic acid	3816Q-01045	1
Caelo	Salicylic acid	16010916	4
Caelo	Salicylic acid	16010923	6
Caelo	Salicylic acid	16312001	21
Caelo	Salicylic acid	16050016	1
Caelo	Salicylic acid	16010922	9
Caelo	Salicylic acid	1601916	1
Caelo	Salicylic acid	8170717	1
Caelo	Salicylic acid	13101707	1
Caelo	Salicylic acid	17133301	13
Caelo	Salicylic acid	163120	1
Caelo	Salicylic acid	16312004	2
Caelo	Salicylic acid	17133304	1
Caelo	Salicylic acid	17301503	17
Caelo	Salicylic acid	1713301	1
Caelo	Salicylic acid	16312008	1
Caelo	Salicylic acid	16312012	2
Caelo	Salicylic acid	17051803	1
Caelo	Salicylic acid	17123301	1
Caelo	Salicylic acid	1801042-01	5
Caelo	Salicylic acid	17301512	9
Caelo	Salicylic acid	18147302	8

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Supplier	Substance	Batch	Spectra
Caelo	Salicylic acid	18147307	1
Caelo	Salicylic acid	19061205	8
Caelo	Salicylic acid	18147321	1
Caelo	Salicylic acid	18230013	1
Caelo	Salicylic acid	11197106	1
Caelo	Salicylic acid	10291803	1
Caelo	Salicylic acid	12323403	3
Caelo	Salicylic acid	160500004	3
Caelo	Salicylic acid	16010972	1
Caelo	Salicylic acid	17301502	14
Caelo	Salicylic acid	RAS1703500	1
Caelo	Salicylic acid	13B14-No1	1
Caelo	Salicylic acid	10355912	1
Caelo	Salicylic acid	14300809	11
Caelo	Salicylic acid	170509AS/16050012	1
Caelo	Salicylic acid	18050002	8
Caelo	Salicylic acid	12374212	2
Caelo	Salicylic acid	14076202	6
Caelo	Salicylic acid	18147308	5
Caelo	Salicylic acid	1234	1
Caelo	Salicylic acid	12134722	4
Caelo	Salicylic acid	1406027	1
Caelo	Salicylic acid	190263	1
Caelo	Salicylic acid	15211809	12
Caelo	Salicylic acid	170301506	1
Caelo	Salicylic acid	12134714	16
Caelo	Salicylic acid	1334403	1
Caelo	Salicylic acid	16050013	18
Caelo	Salicylic acid	18147314	4
Caelo	Salicylic acid	11311905	1
Caelo	Salicylic acid	16010903	9
Caelo	Salicylic acid	16010918	10
Caelo	Salicylic acid	1274210	1
Caelo	Salicylic acid	17301505	22
Caelo	Salicylic acid	72(18230009)	1
Caelo	Salicylic acid	15217304	4
Caelo	Salicylic acid	1509007-01	1
Caelo	Salicylic acid	12134721	2
Caelo	Salicylic acid	12134711	9
Caelo	Salicylic acid	14076203	7
Caelo	Salicylic acid	17301506	33
Caelo	Salicylic acid	1901015-01	2
Caelo	Salicylic acid	16312009	7
Caelo	Salicylic acid	16312010	18
Caelo	Salicylic acid	190612001	1
Caelo	Salicylic acid	18147315	1
Caelo	Salicylic acid	11311923	2
Caelo	Salicylic acid	12134719	3
Caelo	Salicylic acid	14336904	2
Caelo	Salicylic acid	14336906	4
Caelo	Salicylic acid	12374210	3
Caelo	Salicylic acid	13344013	10
Caelo	Salicylic acid	14300808	1
Caelo	Salicylic acid	11311903	1
Caelo	Salicylic acid	RAS1135100	1
Caelo	Salicylic acid	1045	1
Caelo	Salicylic acid	1913Q-01045	1
Caelo	Salicylic acid	12134720	8
Caelo	Salicylic acid	13344003	9
Caelo	Salicylic acid	11197123	4

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Supplier	Substance	Batch	Spectra
Caelo	Salicylic acid	11197118	1
Caelo	Salicylic acid	12134709	23
Caelo	Salicylic acid	1234709	1
Caelo	Salicylic acid	12134715	7
Caelo	Salicylic acid	1303020-01	2
Caelo	Salicylic acid	14076207	10
Caelo	Salicylic acid	14300801	7
Caelo	Salicylic acid	1310516	1
Caelo	Salicylic acid	16010913	14
Caelo	Salicylic acid	16010917	16
Caelo	Salicylic acid	16010910	13
Caelo	Salicylic acid	1605023-01	1
Caelo	Salicylic acid	3944581	1
Caelo	Salicylic acid	16050017	13
Caelo	Salicylic acid	12134710	1
Caelo	Salicylic acid	16050006	1
Caelo	Salicylic acid	18050009	13
Caelo	Salicylic acid	17301612	1
Caelo	Salicylic acid	140602701	1
Caelo	Salicylic acid	12134717	9
Caelo	Salicylic acid	11197103	1
Caelo	Salicylic acid	4010Q-01045	1
Caelo	Salicylic acid	16010912	4
Caelo	Salicylic acid	16010911	4
Caelo	Salicylic acid	16050014	18
Caelo	Salicylic acid	14E26-B04-294622	1
Caelo	Salicylic acid	17133307	37
Caelo	Salicylic acid	12134713	1
Caelo	Salicylic acid	1714Q1045	1
Caelo	Salicylic acid	152117304	1
Caelo	Salicylic acid	14336908	2
Caelo	Salicylic acid	1600917	1
Caelo	Salicylic acid	16/15-B08-332098	1
Caelo	Salicylic acid	17C21-B09-337173	1
Caelo	Salicylic acid	102455-0001	1
Caelo	Salicylic acid	180104201	1
Caelo	Salicylic acid	17301507	13
Caelo	Salicylic acid	18F05-B02-352210	2
Caelo	Salicylic acid	18230009	3
Caelo	Salicylic acid	12036217	2
Caelo	Salicylic acid	1406027-02	2
Caelo	Salicylic acid	15217305	6
Caelo	Salicylic acid	15211808	9
Caelo	Salicylic acid	16010907	6
Caelo	Salicylic acid	15211807	2
Caelo	Salicylic acid	16i15-B08-0001	1
Caelo	Salicylic acid	1707009-01	4
Caelo	Salicylic acid	17C21-B09-337172	1
Caelo	Salicylic acid	18050006	13
Caelo	Salicylic acid	18147303	3
Caelo	Salicylic acid	18230004	9
Caelo	Salicylic acid	18230002	1
Caelo	Salicylic acid	18230007	13
Caelo	Salicylic acid	17301511	2
Caelo	Salicylic acid	15217308	8
Caelo	Salicylic acid	12374207-3454311172	1
Caelo	Salicylic acid	3601413011-12374211	1
Caelo	Salicylic acid	15217303	9
Caelo	Salicylic acid	16I15-B08	1
Caelo	Salicylic acid	15217309	1

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Supplier	Substance	Batch	Spectra
Caelo	Salicylic acid	16312005	20
Caelo	Salicylic acid	17301504	2
Caelo	Salicylic acid	17301509	18
Caelo	Salicylic acid	18147310	4
Caelo	Salicylic acid	18050007	9
caesar	Salicylic acid	15217301	1
Caesar & Loretz GmbH	Salicylic acid	11311922	1
Caesar & Loretz GmbH	Salicylic acid	13344003	1
Caesar & Loretz GmbH	Salicylic acid	14300809	1
Caesar & Loretz GmbH	Salicylic acid	16312001	1
Caesar & Loretz GmbH	Salicylic acid	16312012	1
Caesar & Loretz GmbH	Salicylic acid	17133301	1
Caesar & Loretz GmbH	Salicylic acid	18050006	2
Caesar & Loretz GmbH	Salicylic acid	18050002	1
Caesar & Loretz GmbH	Salicylic acid	17301509	1
Caesar & Loretz GmbH	Salicylic acid	18147302	2
Caesar & Loretz GmbH	Salicylic acid	1847302	1
Caesar & Loretz GmbH	Salicylic acid	18147303	2
Caesar & Loretz GmbH	Salicylic acid	17301512	3
Caesar & Loretz GmbH	Salicylic acid	18230004	1
Caesar & Loretz GmbH	Salicylic acid	18147310	1
Caesar & Loretz GmbH	Salicylic acid	18147308	4
Caesar & Loretz GmbH	Salicylic acid	18147321	2
Caesar & Loretz GmbH	Salicylic acid	19061206	1
Caesar & Loretz GmbH / ...	Salicylic acid	18050006	2
Caesar & Loretz GmbH / ...	Salicylic acid	17301512	1
Caesar & Loretz GmbH / ...	Salicylic acid	19061206	1
Caesar & Loretz GmbH / ...	Salicylic acid	190612004	1
Caesar & Loretz GmbH / ...	Salicylic acid	18147314	3
Caesar & Loretz GmbH D-...	Salicylic acid	11311904	1
Caesar & Loretz GmbH Hi...	Salicylic acid	12134714	1
Caesar & Loretz GmbH, 4...	Salicylic acid	11311917	1
Caesar & Loretz GmbH/ AHD	Salicylic acid	18230004	1
Caesar & Loretz GmbH/Go...	Salicylic acid	18147314	1
Caesar & Loretz/Sanacorp	Salicylic acid	17301503	1
Caesar&Lorenz / Gehe	Salicylic acid	18230004	1
Caesar&Loretz Anzag	Salicylic acid	14300804	2
Caesar&Loretz GmbH,15.0...	Salicylic acid	16312001	1
Caesar&Loretz GmbH/Anzag	Salicylic acid	12374204	1
Caesar&Loretz GmbH/Anzag	Salicylic acid	14076203	2
Caesar&Loretz GmbH/Sana...	Salicylic acid	15217301	1
Caesar&Loretz GmbH/Sana...	Salicylic acid	18230009	1
Caesar&Loretz,Anzag	Salicylic acid	12036211	1
Caesar&Loretz,Phoenix	Salicylic acid	9220710	1
Caesar&Loretz,Phoenix	Salicylic acid	11197104	1
Caesar&Loretz,Phoenix	Salicylic acid	14076212	1
Caesar&Loretz/AHD	Salicylic acid	15211808	1
Caolo- Noweda	Salicylic acid	14300809	2
carlo	Salicylic acid	12134714	2
Cealo	Salicylic acid	15211806	1
Celo/ Sanacorp	Salicylic acid	16010908	1
Delta	Salicylic acid	17133303	1
E Plus	Salicylic acid	16I15-B08-333932	1
Ebert 24.08.16	Salicylic acid	16010903	1
Fagron	Salicylic acid	17301502	1
EuRho	Salicylic acid	1206007-01	2
EuRho	Salicylic acid	1406027-01	2
EuRho	Salicylic acid	1406027-02	1
EuRho	Salicylic acid	1303020-01	1
EuRho	Salicylic acid	1707009-01	1

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Supplier	Substance	Batch	Spectra
EuRho	Salicylic acid	1901015-01	1
EuRho 001	Salicylic acid	1509007-02	1
Eurho/Phoenix	Salicylic acid	13B14-N01	2
Euro	Salicylic acid	1509007-02	2
euro AHD	Salicylic acid	1707009-025709	1
Euro OTC	Salicylic acid	1206007-01	7
Euro OTC	Salicylic acid	1110020	1
Euro OTC	Salicylic acid	1303020-02	4
Euro OTC	Salicylic acid	1406027-02	10
Euro OTC	Salicylic acid	15217301	1
Euro OTC	Salicylic acid	16E02-B09-325356	1
Euro OTC	Salicylic acid	160502331	1
Euro OTC	Salicylic acid	160502302	1
Euro OTC	Salicylic acid	RAS1703500	2
Euro OTC	Salicylic acid	1707009-02	8
Euro OTC	Salicylic acid	1801042-01	22
Euro OTC	Salicylic acid	180104201	4
Euro OTC	Salicylic acid	18050007	1
Euro OTC	Salicylic acid	1901015-01	8
Euro OTC	Salicylic acid	1406027-02Mg1kg	1
Euro OTC	Salicylic acid	14076202	1
Euro OTC	Salicylic acid	115465478596	1
Euro OTC	Salicylic acid	1511023B	1
Euro OTC	Salicylic acid	1509007-01	26
Euro OTC	Salicylic acid	1509007/02	1
Euro OTC	Salicylic acid	1605023/02	1
Euro OTC	Salicylic acid	1303020-01	19
Euro OTC	Salicylic acid	1707009-1	1
Euro OTC	Salicylic acid	1707009	1
Euro OTC	Salicylic acid	1408027	1
Euro OTC	Salicylic acid	1901015-02	1
Euro OTC	Salicylic acid	1605023-02	16
Euro OTC	Salicylic acid	17301509	1
Euro OTC	Salicylic acid	140602702	1
Euro OTC	Salicylic acid	1406027-01	8
Euro OTC	Salicylic acid	170700901	3
Euro OTC	Salicylic acid	170700902	1
Euro OTC	Salicylic acid	1605023-01	17
Euro OTC	Salicylic acid	17133307	1
Euro OTC	Salicylic acid	1509007-02	11
Euro OTC	Salicylic acid	1707009-01	19
Euro OTC	Salicylic acid	14E26-B04-294622	1
Euro OTC	Salicylic acid	160502301	2
Europ Ots Pharma	Salicylic acid	12374205	1
EurRho/ Anzag	Salicylic acid	1509007-01	1
Fagaron	Salicylic acid	14Lo2-B02-303558	1
Fagron	Salicylic acid	17C21-B09	2
Fagron	Salicylic acid	11K10-N01	2
Fagron	Salicylic acid	12C20-N12	5
Fagron	Salicylic acid	11197121	1
Fagron	Salicylic acid	3111Q-01045	1
Fagron	Salicylic acid	12H10-N03	6
Fagron	Salicylic acid	xxxxxxx	1
Fagron	Salicylic acid	102455-0002	1
Fagron	Salicylic acid	13H01-N01	6
Fagron	Salicylic acid	13H01-N08	2
Fagron	Salicylic acid	13H01N01	1
Fagron	Salicylic acid	13H01-N04	13
Fagron	Salicylic acid	13H01N04	4
Fagron	Salicylic acid	13K08-B31-290852	5

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Supplier	Substance	Batch	Spectra
Fagron	Salicylic acid	14B05-B30-290854	5
Fagron	Salicylic acid	14B05-B30	2
Fagron	Salicylic acid	14E26-B04-294623	6
Fagron	Salicylic acid	14E26-B04-294624	6
Fagron	Salicylic acid	11L19-N21	1
Fagron	Salicylic acid	14E26B04	1
Fagron	Salicylic acid	14e26-b04-294623	1
Fagron	Salicylic acid	14E26-B04-294622	1
Fagron	Salicylic acid	14E26-B04-296424	1
Fagron	Salicylic acid	14B05B30	1
Fagron	Salicylic acid	13344013	1
Fagron	Salicylic acid	14E26_B04	1
Fagron	Salicylic acid	14L02-B02-303558	11
Fagron	Salicylic acid	RAS1135100	1
Fagron	Salicylic acid	12c20n12	1
Fagron	Salicylic acid	14L02B02303558	1
Fagron	Salicylic acid	16A18-B04-322905	2
Fagron	Salicylic acid	16/15-B08-330773	3
Fagron	Salicylic acid	16I15-B08-327353	1
Fagron	Salicylic acid	16I15-B08-330773	1
Fagron	Salicylic acid	16I15B08330773	1
Fagron	Salicylic acid	17C21-B09-337173	4
Fagron	Salicylic acid	17c21-b09-337172	1
Fagron	Salicylic acid	17C21B09	1
Fagron	Salicylic acid	16I15-B08-332098	1
Fagron	Salicylic acid	18F05-B02	2
Fagron	Salicylic acid	18F05-B02-351974	1
Fagron	Salicylic acid	18F05-B02-350586	2
Fagron	Salicylic acid	18F05B02350587	2
Fagron	Salicylic acid	18F05-B02-352210	1
Fagron	Salicylic acid	14L02-B02-303557	10
Fagron	Salicylic acid	16A18-B04	1
Fagron	Salicylic acid	18E24-B03-354311	1
Fagron	Salicylic acid	13K08-B31-290853	5
Fagron	Salicylic acid	16A18-B04322904	1
Fagron	Salicylic acid	16/15-B08-332098	2
Fagron	Salicylic acid	RAS1135300	1
Fagron	Salicylic acid	18F05-B02-350587	2
Fagron	Salicylic acid	12C20-N04	1
Fagron	Salicylic acid	17C21-B09-337860	2
Fagron	Salicylic acid	12H10-N08	3
Fagron	Salicylic acid	RAS1818100	1
Fagron	Salicylic acid	14E26-B04	6
Fagron	Salicylic acid	14L02-B02	3
Fagron	Salicylic acid	1140616	1
Fagron	Salicylic acid	18E24-B03	1
Fagron	Salicylic acid	290852	1
Fagron	Salicylic acid	15211809	1
Fagron	Salicylic acid	16/15-B08-333933	1
Fagron	Salicylic acid	14L02B02303557	1
Fagron	Salicylic acid	14E26B04294623	1
Fagron	Salicylic acid	2201115	1
Fagron	Salicylic acid	16A18B04322905	2
Fagron	Salicylic acid	17c21-b09-337860	1
Fagron	Salicylic acid	16A18-B04-322904	2
Fagron	Salicylic acid	16I15-B08	1
Fargon	Salicylic acid	14L02-B02	1
Farmalabor / Farmalabor	Salicylic acid	P1404195-002	1
Fiebig	Salicylic acid	15211810	1
Fiebig	Salicylic acid	16010905	1

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Supplier	Substance	Batch	Spectra
Fiebig	Salicylic acid	17301506	1
Fiebig	Salicylic acid	17301509	1
Fiebig/Maros	Salicylic acid	1707009-02	1
Gatt-Koller	Salicylic acid	1803840	2
gehe	Salicylic acid	16I15-B08-331442	1
Gehe	Salicylic acid	11D15-N08	1
Gehe	Salicylic acid	1050313	1
Gehe	Salicylic acid	1206007-01	1
Gehe	Salicylic acid	13B14-N01	1
Gehe	Salicylic acid	13H01-N04	1
Gehe	Salicylic acid	14L02-B02-303558	1
Gehe	Salicylic acid	165023-02	1
Gehe	Salicylic acid	16010910	1
Gehe	Salicylic acid	17C21-B09-337172	1
Gehe	Salicylic acid	17133307	2
Gehe	Salicylic acid	18F05-B02-350586	1
GEHE	Salicylic acid	1605023-02	2
GEHE	Salicylic acid	1605023-01	1
GEHE	Salicylic acid	1707009-01	1
GEHE	Salicylic acid	1707009-02	1
GEHE	Salicylic acid	17301502	2
GEHE	Salicylic acid	17301511	1
GEHE	Salicylic acid	18230009	1
GEHE	Salicylic acid	18147317	1
Gehe / Spinnrad	Salicylic acid	16050005	1
Caelo	Salicylic acid	17133303	15
Caelo	Salicylic acid	16E02-B09-325355	1
Fagron	Salicylic acid	14e26-B04-294623	1
Gutenberg-Apotheke	Salicylic acid	12374208	1
Holdermann	Salicylic acid	14E26-B04294624	1
Ichthyol	Salicylic acid	11311922	2
Ichthyol/ Noweda	Salicylic acid	17133303	1
Ichthyol/Noweda	Salicylic acid	13344003	1
Jenne	Salicylic acid	12345	1
Kehr	Salicylic acid	16312001	2
Kehr	Salicylic acid	16312012	1
Kehr	Salicylic acid	17301509	1
Klenk	Salicylic acid	12134722	1
Krieger	Salicylic acid	16050012	1
Krieger	Salicylic acid	13032017-MW-A	1
L30	Salicylic acid	16312005	1
L30	Salicylic acid	17301505	1
L30	Salicylic acid	17301507	1
Midas	Salicylic acid	16312010	1
Novacyl	Salicylic acid	1707009-02	1
Novacyl, FR	Salicylic acid	15084403	2
Noweda	Salicylic acid	12036215	1
Noweda	Salicylic acid	12036226	1
Noweda	Salicylic acid	1406027-01	1
Noweda	Salicylic acid	140602702	1
Noweda	Salicylic acid	14336907	2
Noweda	Salicylic acid	16050011	1
Noweda	Salicylic acid	16050013	1
Noweda	Salicylic acid	1707009-02	1
Noweda	Salicylic acid	180104201	1
Noweda/ Infecto Pharm	Salicylic acid	16/15-08-330773	1
Caelo	Salicylic acid	14076212	1
Caelo	Salicylic acid	14336919	21
Caelo	Salicylic acid	160109123	1
Euro OTC	Salicylic acid	102455	1

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Supplier	Substance	Batch	Spectra
Noweda/Fargon	Salicylic acid	14L02-B02-303556	1
Euro OTC	Salicylic acid	130302001	1
Phoenix	Salicylic acid	12H10-No8	1
Phoenix	Salicylic acid	14076201	1
Phoenix	Salicylic acid	15211808	2
Phoenix	Salicylic acid	16050012	1
Phoenix	Salicylic acid	16312005	1
Phoenix	Salicylic acid	17301502	1
Phoenix	Salicylic acid	18050007	1
Phoenix	Salicylic acid	18147308	1
Phoenix goettingen	Salicylic acid	14300808	1
Phoenix/Cealo	Salicylic acid	1733303	1
Phoenix/Cealo	Salicylic acid	3414M-01045	1
Phonix	Salicylic acid	18050007	1
Phönix	Salicylic acid	11311917	1
Phönix	Salicylic acid	12C20-N12	1
Phönix	Salicylic acid	12323401	1
Phönix	Salicylic acid	1303020-01	3
Phönix	Salicylic acid	12374211	1
Phönix	Salicylic acid	12374210	1
Phönix	Salicylic acid	13K08-B31-290853	1
Phönix	Salicylic acid	68/AKD4	1
Phönix	Salicylic acid	1509007-02	1
Phönix	Salicylic acid	16a18-b04-322905	1
Phönix	Salicylic acid	16050005	1
Phönix	Salicylic acid	3177	1
Phönix	Salicylic acid	18050009	2
Caelo	Salicylic acid	16312003	7
Phönix 02.08.2019	Salicylic acid	18230009	1
Phönix Gotha	Salicylic acid	12374207	1
Phönix Gotha	Salicylic acid	14076201	1
Phönix Gotha	Salicylic acid	14300801	1
Caelo	Salicylic acid	11311922	9
Caelo	Salicylic acid	207102017/16050017	1
Fagron	Salicylic acid	17C21-B09-337172	1
Sana 04.02.17 Ek:13,83	Salicylic acid	16010910	1
Sanacorp	Salicylic acid	11311922	1
Sanacorp	Salicylic acid	12134707	1
Sanacorp	Salicylic acid	123036223	1
Sanacorp	Salicylic acid	12374205	1
Sanacorp	Salicylic acid	12134712	1
Sanacorp	Salicylic acid	12374210	1
Sanacorp	Salicylic acid	12134715	1
Sanacorp	Salicylic acid	1303020-01	1
Sanacorp	Salicylic acid	68/AKD2	1
Sanacorp	Salicylic acid	13344014	1
Sanacorp	Salicylic acid	15084404	1
Sanacorp	Salicylic acid	16010910	1
Sanacorp	Salicylic acid	16010912	1
Sanacorp	Salicylic acid	17301506	1
Sanacorp	Salicylic acid	17C21-B09-339446	1
Sanacorp	Salicylic acid	18050006	1
Sanacorp	Salicylic acid	17301509	1
Sanacorp 28.01.15 EK 12...	Salicylic acid	14076204	1
Euro OTC	Salicylic acid	16050013	1
Caelo	Salicylic acid	10355907	1
Caelo	Salicylic acid	12374204	1
Spangropharm	Salicylic acid	11197104	1
VDL	Salicylic acid	11197122	1
Caelo	Salicylic acid	12036202	3

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Supplier	Substance	Batch	Spectra
xxx	Salicylic acid	4311A-01045	1
14076202	Salicylic acid		1
Caelo	Salicylic acid	13344018	19
Caelo	Salicylic acid		5
Caelo	Salicylic acid	13344002	19
EuRho	Salicylic acid		1
Euro OTC	Salicylic acid	1110020-01	4
Euro OTC	Salicylic acid		1
Fagron	Salicylic acid	16I15-B08-333932	2
Fagron	Salicylic acid	190263	1
Fagron	Salicylic acid		1

- 109 266 spectra from 742 *Apo-Ident* customers from a total of 31 508 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Salicylic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Salicylic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	420	0	118 722
Type C	0	1973	8	109 266

The substance/substance group *Salicylic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.5714 %)
Type C	100.0000 % (> 99.8899 %)	99.5962 % (> 99.4447 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Salicylic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ciprofloxacin hydrochloride	38.23	—
Sulfogaiacol hydrate	51.48	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Salicylic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24591	21906	3.79	52.73
20696	21906	4.16	55.28
21436	21906	4.73	55.26
21760	21906	1.50	57.04
21906	21906	0.00	57.36
22443	22443	0.00	56.36
23592	21906	2.00	55.04

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Selenium yeast**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20906-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Selenium yeast

Special notes

When selecting the *Selenium yeast* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Selenium yeast	5	1	3

Second-stage model

For differentiation of the substance/substance group *Selenium yeast* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Selenium yeast*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Selenium yeast	13347911	21377	40	1509355
Caelo	Selenium yeast	17002202	23120	40	1707512
Caelo	Selenium yeast	17002208	23446	40	20170126
Caelo	Selenium yeast	173332	24038	40	20180207*
Euro OTC	Selenium yeast	L1204012-01	20906	40	1403461

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Selenium yeast*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 489 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Selenium yeast*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Selenium yeast	L1401013-01	21102	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 4 spectra from 2 *Apo-Ident* customers from 4 batches from the substance/substance group *Selenium yeast*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Selenium yeast	13347906	1
Caelo	Selenium yeast	15276208	1
Caesar & Loretz GmbH, 4...	Selenium yeast	11318111	1
Caelo	Selenium yeast	13347911	1

- 111 243 spectra from 742 *Apo-Ident* customers from a total of 31 887 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Selenium yeast* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Selenium yeast* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	40	0	119 005
Type C	0	3	1	111 242

The substance/substance group *Selenium yeast* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Selenium yeast* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Calcium glycerophosphate	17.36	—
Calcium citrate tetrahydrate	26.88	—
Polymyxin B sulfate	32.29	—
Menthol	37.40	—
Magnesium citrate	37.76	—
Colistin sulfate	44.93	—
Bacitracin	45.02	—
Amphotericin B	45.28	—
Nystatin	47.70	—
Minoxidil	50.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Selenium yeast* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23120	23120	0.00	25.02
23446	23120	2.57	24.16
24038	24038	0.00	26.46
20906	20906	0.00	36.81
21377	21377	0.00	35.43

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Serine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22289-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Serine; L-serine; Serinum

Special notes

When selecting the *Serine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Serine	6	2	0

Second-stage model

For differentiation of the substance/substance group *Serine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Serine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Serine	1512012	22289	60	20160112*
Euro OTC	Serine	1606020-01	22668	40	20160714
Euro OTC	Serine	1606020	22678	40	20160714*
Euro OTC	Serine	1711033	23914	40	20171208*
Euro OTC	Serine	1904034	24641	40	20190521*
Euro OTC	Serine	1909027	24956	40	20191015*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Serine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Serine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Serine	1611006	22922	40
Euro OTC	Serine	1809016	24296	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Serine*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Serine	1606020-01	3

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Serine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Serine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	74	6	119 062
Type C	0	3	0	111 244

The substance/substance group *Serine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	92.5000 % (> 88.7500 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Serine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	31.73	—
Sodium cromoglicate	54.72	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Serine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22678	22678	0.00	50.67
23914	23914	0.00	52.46
24956	24956	0.00	56.22
24641	24641	0.00	47.50
22289	22289	0.00	50.61
22668	22678	3.09	51.48

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sildenafil citrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20852-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sildenafil citrate; Sildenafil citras

Special notes

When selecting the *Sildenafil citrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sildenafil citrate	7	3	93

Second-stage model

For differentiation of the substance/substance group *Sildenafil citrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sildenafil citrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sildenafil citrate	160498	22446	60	20160307*
Caelo	Sildenafil citrate	170715	23336	40	20170529*
Caelo	Sildenafil citrate	170715	23345	40	20170529*
Euro OTC	Sildenafil citrate	1311010-01	21621	60	20131209
Euro OTC	Sildenafil citrate	1311010-04	23178	40	20150309
Euro OTC	Sildenafil citrate	1908006	24843	40	20190906*
Fagron	Sildenafil citrate	13F24-N03	20852	40	1402052
Fagron	Sildenafil citrate	13J15-N01	20927	80	20131030

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 400 spectra of 8 reference samples from the substance/substance group *Sildenafil citrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 289 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Sildenafil citrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sildenafil citrate	190866	24545	40
Euro OTC	Sildenafil citrate	1807037	24192	40
Euro OTC	Sildenafil citrate	1902031	24469	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 222 spectra from 62 *Apo-Ident* customers from 98 batches from the substance/substance group *Sildenafil citrate*.
- Among them are spectra of independent samples from 92 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sildenafil citrate	17071502	2
Alliance	Sildenafil citrate	1311010-03	1
Caelo	Sildenafil citrate	15097306	1
Caelo	Sildenafil citrate	15097312	2
Caelo	Sildenafil citrate	14074707	2
Caelo	Sildenafil citrate	14074709	1
Caelo	Sildenafil citrate	2101403	1
Caelo	Sildenafil citrate	15F11-B02-314725	1
Caelo	Sildenafil citrate	15097311	1
Caelo	Sildenafil citrate	15097317	1
Caelo	Sildenafil citrate	16049802	10
Caelo	Sildenafil citrate	15097310	1
Caelo	Sildenafil citrate	16049810	2
Caelo	Sildenafil citrate	16049814	9
Caelo	Sildenafil citrate	16049811	1
Caelo	Sildenafil citrate	16049812	1
Caelo	Sildenafil citrate	16049805	1
Caelo	Sildenafil citrate	16049821	8
Caelo	Sildenafil citrate	16049819	1
Caelo	Sildenafil citrate	16049801	1
Caelo	Sildenafil citrate	16049823	2
Caelo	Sildenafil citrate	16049826	1
Caelo	Sildenafil citrate	16049824	1
Caelo	Sildenafil citrate	17071504	15
Caelo	Sildenafil citrate	1734401	1
Caelo	Sildenafil citrate	17344001	1
Caelo	Sildenafil citrate	17344010	1
Caelo	Sildenafil citrate	17344008	1
Caelo	Sildenafil citrate	17344006	1
Caelo	Sildenafil citrate	17344014	1

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Supplier	Substance	Batch	Spectra
Caelo	Sildenafil citrate	19086603	1
Caelo	Sildenafil citrate	19086607	1
Caelo	Sildenafil citrate	16049808	4
Caelo	Sildenafil citrate	15097301	1
Caelo	Sildenafil citrate	17071503	1
Caelo	Sildenafil citrate	16049820	5
Caelo	Sildenafil citrate	14074716	1
Caelo	Sildenafil citrate	14074714	5
Caelo	Sildenafil citrate	14074715	5
Caelo	Sildenafil citrate	101051528	1
Caelo	Sildenafil citrate	19086604	1
Caelo	Sildenafil citrate	1311010-06	1
Caelo	Sildenafil citrate	17344005	3
Caelo	Sildenafil citrate	15097315	1
Caelo	Sildenafil citrate	14074703	2
Caelo	Sildenafil citrate	1407474	1
Caelo	Sildenafil citrate	15097303	1
Caelo	Sildenafil citrate	17344009	1
Caelo	Sildenafil citrate	19086605	5
Caelo	Sildenafil citrate	15F11-B02-309081	1
Caelo	Sildenafil citrate	15097307	2
Caelo	Sildenafil citrate	16049805	1
Euro OTC	Sildenafil citrate	14051402	1
Euro OTC	Sildenafil citrate	17061405	1
Euro OTC	Sildenafil citrate	10061706	1
Euro OTC	Sildenafil citrate	103031328	1
Euro OTC	Sildenafil citrate	1311010	1
Euro OTC	Sildenafil citrate	311010-06	1
Euro OTC	Sildenafil citrate	27021802	1
Euro OTC	Sildenafil citrate	1311010-6	1
Euro OTC	Sildenafil citrate	15081830	1
Euro OTC	Sildenafil citrate	1807037-01	2
Euro OTC	Sildenafil citrate	19011907	1
Euro OTC	Sildenafil citrate	1902031-01	1
Euro OTC	Sildenafil citrate	17081504	1
Euro OTC	Sildenafil citrate	1807037-01x2	1
Euro OTC	Sildenafil citrate	1311010-06	9
Euro OTC	Sildenafil citrate	131101003	1
Euro OTC	Sildenafil citrate	15097301	1
Euro OTC	Sildenafil citrate	1311010-05	5
Euro OTC	Sildenafil citrate	101031827	1
Euro OTC	Sildenafil citrate	131101004	1
Euro OTC	Sildenafil citrate	13110-01	1
Euro OTC	Sildenafil citrate	1311010-03	5
Fagron	Sildenafil citrate	14H11-B01-303183	1
Fagron	Sildenafil citrate	15F11-B02-314725	1
Fagron	Sildenafil citrate	15f11-b02-320186	1
Fagron	Sildenafil citrate	15F11-B02-525175	3
Fagron	Sildenafil citrate	15F11-B02	2
Fagron	Sildenafil citrate	16F30-B02-324715	2
Fagron	Sildenafil citrate	16049817	1
Fagron	Sildenafil citrate	16F30-B02-331450	3
Fagron	Sildenafil citrate	16F30-B02	1
Fagron	Sildenafil citrate	16F30-B02-331449	1
Fagron	Sildenafil citrate	18B13-B06-353827	1
Fagron	Sildenafil citrate	19B07-B02-191472	1
Fagron	Sildenafil citrate	16A18-B08	2
Fagron	Sildenafil citrate	16F30-B02-334977	1
Fagron	Sildenafil citrate	17H31-B02-342459	3
Fagron	Sildenafil citrate	16049812	1

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Supplier	Substance	Batch	Spectra
Fagron	Sildenafil citrate	16049819	2
Fagron	Sildenafil citrate	17071505	1
Gehe	Sildenafil citrate	13F24-N03	1
Gehe	Sildenafil citrate	16049805	1
Gehe	Sildenafil citrate	17344008	1
GEHE	Sildenafil citrate	17344003	1
Gutenberg-Apotheke	Sildenafil citrate	1311010-01	1
Noweda	Sildenafil citrate	18B13-B06-348002	1
Noweda	Sildenafil citrate	19086603	1
Noweda	Sildenafil citrate	19086607	1
Noweda/ Caesar & Loretz...	Sildenafil citrate	19086607	1
Fagron	Sildenafil citrate	16F30-B02-324715	1
Caelo	Sildenafil citrate	19086606	1
Fagron	Sildenafil citrate	15F11-B02-320186	1
Phoenix	Sildenafil citrate	1311010-04	2
Phönix/Polpharma	Sildenafil citrate	1311010-01	1
Polpharma/Phoenix	Sildenafil citrate	131101001	1
Sanacorp	Sildenafil citrate	14H11-B01-297519	2
Sanacorp	Sildenafil citrate	16049811	2
Caelo	Sildenafil citrate	17344003	3
Sanacorp WE 21.04.17 -2...	Sildenafil citrate	16049808	1
Caelo	Sildenafil citrate	17344004	2
Alliance	Sildenafil citrate		1
Euro OTC	Sildenafil citrate	1311010-04	2
Euro OTC	Sildenafil citrate	1311010-01	4
Fagron	Sildenafil citrate	13J15-N01	2
	Sildenafil citrate	1311010-04	2

- 111 025 spectra from 742 *Apo-Ident* customers from a total of 31 793 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sildenafil citrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sildenafil citrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	400	0	110 289
Type B	0	120	0	119 022
Type C	0	222	0	111 025

The substance/substance group *Sildenafil citrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 97.2973 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sildenafil citrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxybuprocaine hydrochloride	57.61	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sildenafil citrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20852	20852	0.00	63.99
20927	20852	2.17	63.12
21621	24843	4.09	61.29
23178	23336	7.30	61.81
23336	23336	0.00	62.30
23345	23345	0.00	61.60
24843	24843	0.00	63.59
22446	22446	0.00	63.08

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium acetate trihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20984-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium acetate trihydrate; Natrii acetat trihydricum

Special notes

When selecting the *Sodium acetate trihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium acetate trihydrate	6	5	22

Second-stage model

For differentiation of the substance/substance group *Sodium acetate trihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium acetate trihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium acetate t...	12316506	20984	40	1402111
Caelo	Sodium acetate t...	13411404	21441	60	20140113
Caelo	Sodium acetate t...	172003	23812	40	20171107*
Euro OTC	Sodium acetate t...	1507020	21861	60	20150723*
Euro OTC	Sodium acetate t...	1706008	23547	40	20170710*
Euro OTC	Sodium acetate t...	2002041	25131	40	20200331*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Sodium acetate trihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Sodium acetate trihydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium acetate trihydrate	163007	22760	40
Caelo	Sodium acetate trihydrate	183152	24370	40
Euro OTC	Sodium acetate trihydrate	1608032	22802	40
Euro OTC	Sodium acetate trihydrate	1901026	24595	40
Euro OTC	Sodium acetate trihydrate	1906023	24811	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 56 spectra from 35 *Apo-Ident* customers from 23 batches from the substance/substance group *Sodium acetate trihydrate*.
- Among them are spectra of independent samples from 22 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium acetate trihydrate	12027202	1
Caelo	Sodium acetate trihydrate	10353017	1
Caelo	Sodium acetate trihydrate	15118701	5
Caelo	Sodium acetate trihydrate	15145204	5
Caelo	Sodium acetate trihydrate	15145205	1
Caelo	Sodium acetate trihydrate	16300706	4
Caelo	Sodium acetate trihydrate	16300711	9
Caelo	Sodium acetate trihydrate	18173602	1
Caelo	Sodium acetate trihydrate	18315203	1
Caelo	Sodium acetate trihydrate	12027217	1
Caelo	Sodium acetate trihydrate	15145209	5
Caelo	Sodium acetate trihydrate	16300705	1
Caelo	Sodium acetate trihydrate	12027228	1
Caelo	Sodium acetate trihydrate	151452009	1
Caelo	Sodium acetate trihydrate	12316501	1
Caelo	Sodium acetate trihydrate	15145218	2
Caelo	Sodium acetate trihydrate	13411418	2
Caelo	Sodium acetate trihydrate	16300712	1
Caelo	Sodium acetate trihydrate	13295606	1
Caelo	Sodium acetate trihydrate	13295601	1
Caesar & Lorenz GmbH	Sodium acetate trihydrate	16300706	1
Ebert KKH 13.10.16	Sodium acetate trihydrate	15145204	1
Ebert KKH 13.10.16	Sodium acetate trihydrate	15145209	1
Euro OTC	Sodium acetate trihydrate	1005020V-01	1
Caelo	Sodium acetate trihydrate	18006801	5
Phönix Gotha	Sodium acetate trihydrate	12316506	1
Sanacorp	Sodium acetate trihydrate	13295601	1

- 111 191 spectra from 742 *Apo-Ident* customers from a total of 31 868 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium acetate trihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium acetate trihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	200	0	118 942
Type C	0	54	2	111 191

The substance/substance group *Sodium acetate trihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	96.4286 % (> 91.0714 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium acetate trihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	32.83	—
Sodium tetraborate	33.77	—
Sodium cromoglicate	49.17	—
Polymyxin B sulfate	63.52	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium acetate trihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20984	20984	0.00	38.40
21441	20984	2.82	38.92
21861	21861	0.00	36.74
23547	23547	0.00	37.76
23812	23812	0.00	38.53
25131	25131	0.00	40.56

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium ascorbate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20520-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium ascorbate; Natrii ascorbas

Special notes

When selecting the *Sodium ascorbate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium ascorbate	7	19	27

Second-stage model

For differentiation of the substance/substance group *Sodium ascorbate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium ascorbate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium ascorbate	15429905	22899	40	20160118
Caelo	Sodium ascorbate	182620	24386	40	20181112*
Euro OTC	Sodium ascorbate	1406018-01	21583	60	1411165
Euro OTC	Sodium ascorbate	1406018-01	21789	60	20140724
Euro OTC	Sodium ascorbate	1507030	21853	60	20150811*
Euro OTC	Sodium ascorbate	1506018	21865	60	20150706*
Euro OTC	Sodium ascorbate	1510017	21946	60	20151102*
Euro OTC	Sodium ascorbate	1601007	22304	60	20160120*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 440 spectra of 8 reference samples from the substance/substance group *Sodium ascorbate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 249 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 880 spectra of 22 reference samples from the substance/substance group *Sodium ascorbate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 19 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium ascorbate	162857	22761	40
Caelo	Sodium ascorbate	172235	23809	40
Caelo	Sodium ascorbate	180326	24029	40
Caelo	Sodium ascorbate	191393	24751	40
Caelo	Sodium ascorbate	192304	24896	40
Euro OTC	Sodium ascorbate	1604001	22524	40
Euro OTC	Sodium ascorbate	1607044	22690	40
Euro OTC	Sodium ascorbate	1611015	22864	40
Euro OTC	Sodium ascorbate	1701054	23134	40
Euro OTC	Sodium ascorbate	1703012	23152	40
Euro OTC	Sodium ascorbate	1705013	23430	40
Euro OTC	Sodium ascorbate	1705014	23432	40
Euro OTC	Sodium ascorbate	1803005	24069	40
Euro OTC	Sodium ascorbate	1807043	24149	40
Euro OTC	Sodium ascorbate	1811002	24337	40
Euro OTC	Sodium ascorbate	1902021	24460	40
Euro OTC	Sodium ascorbate	1906005	24786	40
Euro OTC	Sodium ascorbate	1906004	24807	40
Euro OTC	Sodium ascorbate	1908026	24930	40
Euro OTC	Sodium ascorbate	1906004	24935	40
Euro OTC	Sodium ascorbate	1902021	24943	40
Euro OTC	Sodium ascorbate	1906005	24976	40

- 118 262 spectra from a total of 2401 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 29 spectra from 9 *Apo-Ident* customers from 27 batches from the substance/substance group *Sodium ascorbate*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium ascorbate	27091302	1
Caelo	Sodium ascorbate	1604001-01	1
Caelo	Sodium ascorbate	16285710	1
Caelo	Sodium ascorbate	15429917	1
Caelo	Sodium ascorbate	17223504	1
Caelo	Sodium ascorbate	17356201	1
Caesar & Loretz GmbH	Sodium ascorbate	18262001	1
Caesar & Loretz GmbH	Sodium ascorbate	18262009	1
Euro OTC	Sodium ascorbate	16091301	1
Euro OTC	Sodium ascorbate	20091303	1
Euro OTC	Sodium ascorbate	4021401	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Sodium ascorbate	13031402	1
Euro OTC	Sodium ascorbate	13051406	1
Euro OTC	Sodium ascorbate	12061407	1
Euro OTC	Sodium ascorbate	11081401	1
Euro OTC	Sodium ascorbate	170105401	1
Euro OTC	Sodium ascorbate	1703012-01	1
Euro OTC	Sodium ascorbate	L1308005-01	1
Euro OTC	Sodium ascorbate	1210026-01	1
Fagron	Sodium ascorbate	12L27-N03	1
Fagron	Sodium ascorbate	13C15-N01	1
Gatt-Koller	Sodium ascorbate	1802317	3
Caelo	Sodium ascorbate	15180505	1
Caelo	Sodium ascorbate	14079404	1
Euro OTC	Sodium ascorbate	28081304	1
Euro OTC	Sodium ascorbate	11121301	1
Euro OTC	Sodium ascorbate	7011405	1

- 111 218 spectra from 742 *Apo-Ident* customers from a total of 31 864 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium ascorbate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium ascorbate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	440	0	110 249
Type B	0	880	0	118 262
Type C	0	29	0	111 218

The substance/substance group *Sodium ascorbate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6364 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.3182 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 79.3103 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium ascorbate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	66.03	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium ascorbate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22899	22304	1.58	76.03
21946	21946	0.00	77.59
22304	22304	0.00	75.24
21583	21583	0.00	78.82
21789	21865	3.20	76.80
21853	21853	0.00	77.53
21865	21865	0.00	76.12
24386	24386	0.00	77.30

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium benzoate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20479-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium benzoate; Natrii benzoas

Special notes

When selecting the *Sodium benzoate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium benzoate	10	10	116

Second-stage model

For differentiation of the substance/substance group *Sodium benzoate* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium benzoate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium benzoate	11267016	20752	40	20110923
Caelo	Sodium benzoate	13178619	21607	60	20130624
Euro OTC	Sodium benzoate	1409040-01	21713	60	20141021
Euro OTC	Sodium benzoate	1506019	21825	60	20150623*
Euro OTC	Sodium benzoate	1510044	22236	60	20151109*
Euro OTC	Sodium benzoate	1602020	22363	60	20160225*
Euro OTC	Sodium benzoate	1610037	22867	40	20161202*
Euro OTC	Sodium benzoate	1701045	22997	40	20170207*
Euro OTC	Sodium benzoate	1711019	23900	40	20171205*
Euro OTC	Sodium benzoate	2001018	25081	40	20200205*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 10 reference samples from the substance/substance group *Sodium benzoate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 189 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 420 spectra of 10 reference samples from the substance/substance group *Sodium benzoate*.
- Among them are spectra of independent samples from 10 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium benzoate	161371	22474	60
Caelo	Sodium benzoate	170558	23283	40
Caelo	Sodium benzoate	173530	23784	40
Caelo	Sodium benzoate	190541	24544	40
Euro OTC	Sodium benzoate	1607005	22670	40
Euro OTC	Sodium benzoate	1707024	23613	40
Euro OTC	Sodium benzoate	1803034	24068	40
Euro OTC	Sodium benzoate	1809005	24301	40
Euro OTC	Sodium benzoate	1901043	24481	40
Fagron	Sodium benzoate	15B16-B07-308570	22895	40

- 118 722 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 347 spectra from 217 *Apo-Ident* customers from 121 batches from the substance/substance group *Sodium benzoate*.
- Among them are spectra of independent samples from 116 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Sodium benzoate	17137606	1
AHD	Sodium benzoate	1711019-01	3
Alliance Healthcare	Sodium benzoate	1304024-01	1
Bombastus	Sodium benzoate	1404011-01	1
Bombastus	Sodium benzoate	17055805	1
Bombastus	Sodium benzoate	17353011	1
Caelo	Sodium benzoate	12158401	1
Caelo	Sodium benzoate	12158419	4
Caelo	Sodium benzoate	17061306	1
Caelo	Sodium benzoate	12158418	1
Caelo	Sodium benzoate	13178605	3
Caelo	Sodium benzoate	13178627	1
Caelo	Sodium benzoate	13178647	2
Caelo	Sodium benzoate	24021501	1
Caelo	Sodium benzoate	14328702	1
Caelo	Sodium benzoate	1506019-01	1
Caelo	Sodium benzoate	15363401	10
Caelo	Sodium benzoate	11346109	3
Caelo	Sodium benzoate	15363413	2
Caelo	Sodium benzoate	10544104	1
Caelo	Sodium benzoate	151208NB	1

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Supplier	Substance	Batch	Spectra
Caelo	Sodium benzoate	91443209	2
Caelo	Sodium benzoate	16137104	2
Caelo	Sodium benzoate	16137103	8
Caelo	Sodium benzoate	161371	1
Caelo	Sodium benzoate	17055801	5
Caelo	Sodium benzoate	16137118	7
Caelo	Sodium benzoate	1610037-01	1
Caelo	Sodium benzoate	17137606	12
Caelo	Sodium benzoate	17137609	1
Caelo	Sodium benzoate	NB20180313	1
Caelo	Sodium benzoate	17353002	1
Caelo	Sodium benzoate	19091801	1
Caelo	Sodium benzoate	19054114	1
Caelo	Sodium benzoate	17353001	8
Caelo	Sodium benzoate	3037647	1
Caelo	Sodium benzoate	13178603	2
Caelo	Sodium benzoate	14166714	1
Caelo	Sodium benzoate	5117A-01891	1
Caelo	Sodium benzoate	17137604	3
Caelo	Sodium benzoate	15044102	6
Caelo	Sodium benzoate	15363409	2
Caelo	Sodium benzoate	18161211	9
Caelo	Sodium benzoate	12J23-N05	1
Caelo	Sodium benzoate	18161201	6
Caelo	Sodium benzoate	12158439	3
Caelo	Sodium benzoate	1209018-0	1
Caelo	Sodium benzoate	17353011	2
Caelo	Sodium benzoate	19054104	4
Caelo	Sodium benzoate	17055806	1
Caelo	Sodium benzoate	18055805	1
Caelo	Sodium benzoate	12158424	1
Caelo	Sodium benzoate	15044104	8
Caelo	Sodium benzoate	15135001	6
Caelo	Sodium benzoate	15363424	10
Caelo	Sodium benzoate	15363414	1
Caelo	Sodium benzoate	17353006	2
Caelo	Sodium benzoate	5211I-01891	1
Caelo	Sodium benzoate	1503022-01	1
Caelo	Sodium benzoate	2215Q-01891	1
Caelo	Sodium benzoate	4315A-01891	1
Caelo	Sodium benzoate	17055805	5
Caelo	Sodium benzoate	13178613	1
Caelo	Sodium benzoate	13178635	5
Caelo	Sodium benzoate	16137112	6
calo	Sodium benzoate	17055805	1
Euro OTC	Sodium benzoate	1307013-01	2
EuRho	Sodium benzoate	1112006-01	1
EuRho Anzag	Sodium benzoate	1304024-01	1
Euro OCT / Noweda	Sodium benzoate	1510044-01	1
Euro OTC	Sodium benzoate	171101901	1
Euro OTC	Sodium benzoate	180900501	2
Euro OTC	Sodium benzoate	130402401	2
Euro OTC	Sodium benzoate	1404011-01	4
Euro OTC	Sodium benzoate	15363424	1
Euro OTC	Sodium benzoate	1803034-01	2
Euro OTC	Sodium benzoate	1809005-01	8
Euro OTC	Sodium benzoate	1901043-01	5
Euro OTC	Sodium benzoate	1901043-02	5
Euro OTC	Sodium benzoate	16137112	1
Euro OTC	Sodium benzoate	1209018-01	4

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Supplier	Substance	Batch	Spectra
Euro OTC	Sodium benzoate	1701045-01	2
Euro OTC	Sodium benzoate	1607005-01	5
Euro OTC	Sodium benzoate	1209018-18	1
Euro OTC	Sodium benzoate	170702401	1
Euro OTC	Sodium benzoate	1506019-01	6
Euro/ Phönix	Sodium benzoate	1404011-01	1
Euro OTC	Sodium benzoate	151004401	4
Euro OTC	Sodium benzoate	15060119-01	1
Euro OTC	Sodium benzoate	2604040V-05	1
Euro OTC	Sodium benzoate	1309027-01	2
Euro OTC	Sodium benzoate	1610037-01	3
Euro OTC	Sodium benzoate	1711019-01	2
EuroTOC / Noweda	Sodium benzoate	130902701	1
Fagron	Sodium benzoate	12G04-N04	1
Fagron	Sodium benzoate	12J23-N05	3
Fagron	Sodium benzoate	13C14-N01	4
Fagron	Sodium benzoate	24011401	1
Fagron	Sodium benzoate	13I27-B03288805	1
Fagron	Sodium benzoate	13/27-B03-288805	1
Fagron	Sodium benzoate	13H01-N02	1
Fagron	Sodium benzoate	13I27-B03-288806	1
Fagron	Sodium benzoate	13/27B03288805	1
Fagron	Sodium benzoate	13/27b03288805	1
Fagron	Sodium benzoate	14E12Bo7296717	1
Fagron	Sodium benzoate	14E12B07296717	1
Fagron	Sodium benzoate	14E12B07296717	1
Fagron	Sodium benzoate	14E12-B07	1
Fagron	Sodium benzoate	15B16-B07-306571	2
Fagron	Sodium benzoate	15B16-B07	1
Fagron	Sodium benzoate	1412	1
Fagron	Sodium benzoate	15363403	1
Fagron	Sodium benzoate	1602020-01	1
Fagron	Sodium benzoate	12D02-N06	1
Fagron	Sodium benzoate	test	1
Fagron	Sodium benzoate	12C05-N04	1
Fagron	Sodium benzoate	15B16-B07-308570	1
Fagron	Sodium benzoate	12H08-N06	1
Fagron	Sodium benzoate	14E12-B07-306570	1
Fagron	Sodium benzoate	16B23-B06-322528	1
Fagron	Sodium benzoate	13C14-N01	1
Fiebig 27.06.13 EK3,34	Sodium benzoate	1304024-01	1
Gehe	Sodium benzoate	1610037-01	1
Gehe	Sodium benzoate	1707024-01	2
Gehe	Sodium benzoate	18161211	7
GEHE	Sodium benzoate	17137606	1
Euro OTC	Sodium benzoate	1510044-01	12
Hedinger	Sodium benzoate	13I27-B03	1
Hedinger/Phönix	Sodium benzoate	15363413	1
Caelo	Sodium benzoate	192296003	1
Kehr	Sodium benzoate	1701045-01	1
Nachtestung	Sodium benzoate	300/18	1
Nokun	Sodium benzoate	17137606	2
Noweda	Sodium benzoate	1209018-01	1
Noweda	Sodium benzoate	16137103	1
Noweda	Sodium benzoate	1711019-01	1
Noweda	Sodium benzoate	189005-01	1
Euro OTC	Sodium benzoate	1007019-01	1
Euro OTC	Sodium benzoate	1602020-01	2
Fagron	Sodium benzoate	13I27-B03-288806	3
Euro OTC	Sodium benzoate	190104301	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Sodium benzoate	1112006-01	1
Phoenix goettin	Sodium benzoate	13I27-B03-288806	1
Phönix	Sodium benzoate	1510044/01	1
Phönix	Sodium benzoate	17137606	1
sana	Sodium benzoate	13178635	1
Euro OTC	Sodium benzoate	1304024-01	5
Unisan	Sodium benzoate	1404011-01	1
Caelo	Sodium benzoate	13178619	2
Caelo	Sodium benzoate	11267016	1
Euro OTC	Sodium benzoate	1409040-01	1
Euro OTC	Sodium benzoate	1701045	1

- 110 900 spectra from 742 *Apo-Ident* customers from a total of 31 771 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium benzoate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium benzoate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	500	0	110 189
Type B	0	420	0	118 722
Type C	0	338	9	110 900

The substance/substance group *Sodium benzoate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.5714 %)
Type C	100.0000 % (> 99.8899 %)	97.4063 % (> 96.5418 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium benzoate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Diclofenac sodium	39.83	—
Ciprofloxacin hydrochloride	50.42	—
⋮	⋮	⋮
Beclometasone dipropionate	>50	283.37
Betamethasone dipropionate, micronized	>50	343.08
Clobetasol propionate	>50	346.67
Gentamicin sulfate	>50	353.71
Oxybutynin hydrochloride	>50	448.18
Sodium citrate	>50	677.75

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium benzoate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23900	23900	0.00	56.94
22997	22997	0.00	58.38
21713	22236	4.35	57.62
22236	22236	0.00	56.19
21607	23900	6.60	58.34
21825	21825	0.00	54.71
22867	22867	0.00	58.45
25081	25081	0.00	58.00
22363	22363	0.00	59.11
20752	22236	6.76	57.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium citrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20662-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium citrate; Natrii citras

Special notes

When selecting the *Sodium citrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium citrate	10	13	256

Second-stage model

For differentiation of the substance/substance group *Sodium citrate* the following second-stage model is used:

- [Submodel 2](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium citrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium citrate	12045026	20918	40	20120307
Caelo	Sodium citrate	13089335	21670	60	AR-15-FG-000405-01
Caelo	Sodium citrate	14112517	21718	60	20140416
Euro OTC	Sodium citrate	1506041	21839	60	0000010492
Euro OTC	Sodium citrate	1511017	21997	60	20151130*
Euro OTC	Sodium citrate	1610016	22859	40	20161102*
Euro OTC	Sodium citrate	1701029	22996	40	20170126*
Fagron	Sodium citrate	12E04-N05	20662	40	20120516
Fagron	Sodium citrate	14A13-B02-294541	21778	60	20140424
Fagron	Sodium citrate	16F10-B01-326088	22843	40	20160711

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 500 spectra of 10 reference samples from the substance/substance group *Sodium citrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 189 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 520 spectra of 13 reference samples from the substance/substance group *Sodium citrate*.
- Among them are spectra of independent samples from 13 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium citrate	12045008	20656	40
Caelo	Sodium citrate	162179	22618	40
Caelo	Sodium citrate	173236	23789	40
Caelo	Sodium citrate	182083	24218	40
Caelo	Sodium citrate	190890	24533	40
Euro OTC	Sodium citrate	1205026-01	20652	40
Euro OTC	Sodium citrate	1604030	22510	40
Euro OTC	Sodium citrate	1607040	22687	40
Euro OTC	Sodium citrate	1710006	23614	40
Euro OTC	Sodium citrate	1807035	24151	40
Euro OTC	Sodium citrate	1901035	24487	40
Euro OTC	Sodium citrate	1909020	24862	40
Euro OTC	Sodium citrate	2002040	25127	40

- 118 622 spectra from a total of 2407 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1089 spectra from 474 *Apo-Ident* customers from 264 batches from the substance/substance group *Sodium citrate*.
- Among them are spectra of independent samples from 256 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Sodium citrate	1607040-01	2
AHD	Sodium citrate	1710006-01	2
AHD	Sodium citrate	17323602	1
Alliance Healthcare	Sodium citrate	1211030-01	1
Anzag	Sodium citrate	1512705	1
Fagron	Sodium citrate	12J26-N02	2
ApoIdent/ Phoenix	Sodium citrate	1710006-01	1
Audor Pharma	Sodium citrate	171000601	1
Aug. Hedinger	Sodium citrate	8765456	1
Bombastus	Sodium citrate	73155098	1
Caelo	Sodium citrate	12045019	4
Caelo	Sodium citrate	14369402	2
Caelo	Sodium citrate	test13	1
Caelo	Sodium citrate	Test123	1
Caelo	Sodium citrate	2815A-01900	1
Caelo	Sodium citrate	12045002	1
Caelo	Sodium citrate	12045006	1
Caelo	Sodium citrate	12045008	3

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Supplier	Substance	Batch	Spectra
Caelo	Sodium citrate	1234	3
Caelo	Sodium citrate	12045001	1
Caelo	Sodium citrate	21121203	1
Caelo	Sodium citrate	12045016	5
Caelo	Sodium citrate	1151351	2
Caelo	Sodium citrate	K-280313-1	1
Caelo	Sodium citrate	25383143	1
Caelo	Sodium citrate	13089304	2
Caelo	Sodium citrate	12045012	1
Caelo	Sodium citrate	1308908	1
Caelo	Sodium citrate	11121303	1
Caelo	Sodium citrate	70214PJK01	1
Caelo	Sodium citrate	13089317	7
Caelo	Sodium citrate	13089331	5
Caelo	Sodium citrate	12897	1
Caelo	Sodium citrate	123Test	9
Caelo	Sodium citrate	131103501	1
Caelo	Sodium citrate	1411502	1
Caelo	Sodium citrate	13089319	4
Caelo	Sodium citrate	220914PML01	1
Caelo	Sodium citrate	4680	1
Caelo	Sodium citrate	1404033-01	3
Caelo	Sodium citrate	13089314	1
Caelo	Sodium citrate	14112520	1
Caelo	Sodium citrate	123e2	1
Caelo	Sodium citrate	14369406	6
Caelo	Sodium citrate	50815PMS01	1
Caelo	Sodium citrate	123test	4
Caelo	Sodium citrate	1223test	1
Caelo	Sodium citrate	1412014-01	1
Caelo	Sodium citrate	14369411	3
Caelo	Sodium citrate	1234Test	3
Caelo	Sodium citrate	14369413	18
Caelo	Sodium citrate	11081514	1
Caelo	Sodium citrate	17081501	1
Caelo	Sodium citrate	Test	2
Caelo	Sodium citrate	14112518	1
Caelo	Sodium citrate	14369415	1
Caelo	Sodium citrate	2543	1
Caelo	Sodium citrate	123tst	1
Caelo	Sodium citrate	14369424	4
Caelo	Sodium citrate	140510/1	1
Caelo	Sodium citrate	123456789	1
Caelo	Sodium citrate	1123588946	1
Caelo	Sodium citrate	14369416	1
Caelo	Sodium citrate	123456	1
Caelo	Sodium citrate	123658	1
Caelo	Sodium citrate	459842	1
Caelo	Sodium citrate	1256825	1
Caelo	Sodium citrate	14838	1
Caelo	Sodium citrate	128896	1
Caelo	Sodium citrate	154662	1
Caelo	Sodium citrate	125874566	1
Caelo	Sodium citrate	TestmessungnachRep	1
Caelo	Sodium citrate	140731NC	1
Caelo	Sodium citrate	2345678	1
Caelo	Sodium citrate	15212705	4
Caelo	Sodium citrate	1610016-01	3
Caelo	Sodium citrate	16217901	1
Caelo	Sodium citrate	14360407	1

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Supplier	Substance	Batch	Spectra
Caelo	Sodium citrate	16F10-B01-326093	1
Caelo	Sodium citrate	16217908	1
Caelo	Sodium citrate	17H7-B04-345098	1
Caelo	Sodium citrate	1732361	1
Caelo	Sodium citrate	17323609	2
Caelo	Sodium citrate	17323602	2
Caelo	Sodium citrate	30081802	1
Caelo	Sodium citrate	1732608	1
Caelo	Sodium citrate	19121802	1
Caelo	Sodium citrate	2908022-01	1
Caelo	Sodium citrate	18208307	7
Caelo	Sodium citrate	19089004	2
Caelo	Sodium citrate	12045024	5
Caelo	Sodium citrate	16217909	6
Caelo	Sodium citrate	11219012	3
Caelo	Sodium citrate	16095707	6
Caelo	Sodium citrate	171025NC/16217909	1
Caelo	Sodium citrate	16217912	4
Caelo	Sodium citrate	3040611	1
Caelo	Sodium citrate	18208315	13
Caelo	Sodium citrate	13089308	7
Caelo	Sodium citrate	1701029-01	4
Caelo	Sodium citrate	151101701	1
Caelo	Sodium citrate	19089003	2
Caelo	Sodium citrate	1607040-01	4
Caelo	Sodium citrate	171006-02	1
Caelo	Sodium citrate	18208302	9
Caelo	Sodium citrate	1807035-01	2
Caelo	Sodium citrate	Testmessung	1
Caelo	Sodium citrate	15C27-B01-309893	1
Caelo	Sodium citrate	2413A-01900	1
Caelo	Sodium citrate	16217902	1
Caelo	Sodium citrate	49131-01900	1
Caelo	Sodium citrate	14112502	22
Caelo	Sodium citrate	14369407	40
Caelo	Sodium citrate	16095702	3
Caelo	Sodium citrate	1807035-02	1
Caelo	Sodium citrate	13089305	1
Caelo	Sodium citrate	17323601	23
Caelo	Sodium citrate	12045011	6
Caelo	Sodium citrate	11304311	3
Caelo	Sodium citrate	13089329	1
Caelo	Sodium citrate	1042	1
Caelo	Sodium citrate	12358Test	1
Caelo	Sodium citrate	16217905	13
Caelo	Sodium citrate	16F10-B01-327510	1
Caelo	Sodium citrate	16217914	3
Caelo	Sodium citrate	1732601	1
Caelo	Sodium citrate	17323612	1
Fagron	Sodium citrate	1807035-01	1
Caelo	Sodium citrate	4111Q-01900	1
Caelo	Sodium citrate	160704001	1
Caelo	Sodium citrate	13089325	3
Caelo	Sodium citrate	1161207	2
Caelo	Sodium citrate	13/24-B13-287921	1
Caelo	Sodium citrate	1506041-01	1
Caelo	Sodium citrate	16217906	1
Caelo	Sodium citrate	16217913	1
Caelo	Sodium citrate	14369414	1
Caelo	Sodium citrate	12045016-3451311172	1

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Supplier	Substance	Batch	Spectra
Caelo	Sodium citrate	1107011-01	1
Caelo	Sodium citrate	14369423	17
Caelo	Sodium citrate	12045004	3
Caesar & Loretz GmbH	Sodium citrate	13089334	1
Caesar & Loretz GmbH	Sodium citrate	14112517	1
Caesar & Loretz GmbH	Sodium citrate	14369406	1
Caesar & Loretz GmbH	Sodium citrate	18208302	2
Caesar & Loretz GmbH	Sodium citrate	18208307	1
Caesar & Loretz GmbH / ...	Sodium citrate	14369406	1
Caesar & Loretz GmbH / ...	Sodium citrate	18208302	1
Caesar & Loretz GmbH/ AHD	Sodium citrate	18208315	1
Caesar & Loretz GmbH/An...	Sodium citrate	19089003	1
Caesar&Loretz GmbH	Sodium citrate	12045026	1
Caesar&Loretz GmbH	Sodium citrate	14112502	1
Caesar&Loretz GmbH/Anzag	Sodium citrate	14369407	1
Caesar/Noweda	Sodium citrate	12045008	1
Caeser und Loretz GmbH	Sodium citrate	18208308	1
Delta Apotheke	Sodium citrate	17323608	1
EuRho	Sodium citrate	1107011-02	1
EuRho	Sodium citrate	4611M-01900	1
EuRho	Sodium citrate	1205026-02	1
EuRho	Sodium citrate	1311035-01	1
EuRho	Sodium citrate	140403301	1
EuRho	Sodium citrate	1211030-01	1
EuRho	Sodium citrate	1412014-01	1
EuRho	Sodium citrate	1607040-01	5
EuRho	Sodium citrate	3032981	1
EuRho	Sodium citrate	1070102901	1
EuRho	Sodium citrate	1901035-01	1
EuRho / Phoenix	Sodium citrate	151101017-01	1
EuRho/Sanacorp	Sodium citrate	1107011-02	1
EuRho/Sanacorp	Sodium citrate	1506041-01	1
Euro	Sodium citrate	1815M-01900	1
Euro OTC	Sodium citrate	20200810-6	1
Euro OTC	Sodium citrate	1413M-01900	1
Euro OTC	Sodium citrate	1211030-01	10
Euro OTC	Sodium citrate	2903001-01	1
Euro OTC	Sodium citrate	22101305	1
Euro OTC	Sodium citrate	1073240	1
Euro OTC	Sodium citrate	17061407	1
Euro OTC	Sodium citrate	1506041-01	16
Euro OTC	Sodium citrate	345678	1
Euro OTC	Sodium citrate	1610016601	1
Euro OTC	Sodium citrate	1701029-01	29
Euro OTC	Sodium citrate	4716E-01900	1
Euro OTC	Sodium citrate	1701029-02	1
Euro OTC	Sodium citrate	1710006-02	7
Euro OTC	Sodium citrate	30611044	1
Euro OTC	Sodium citrate	3032805	2
Euro OTC	Sodium citrate	16070-01	1
Euro OTC	Sodium citrate	1909020-01	4
Euro OTC	Sodium citrate	140403301	4
Euro OTC	Sodium citrate	1511017-01	27
Euro OTC	Sodium citrate	1710006-01	8
Euro OTC	Sodium citrate	151101701	2
Euro OTC	Sodium citrate	1311035-01	23
Euro OTC	Sodium citrate	14201401	1
Euro OTC	Sodium citrate	23062015C	1
Euro OTC	Sodium citrate	15212705	1
Euro OTC	Sodium citrate	1807035-01	14

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Supplier	Substance	Batch	Spectra
Euro OTC	Sodium citrate	1205026-02	4
Euro OTC	Sodium citrate	1807035-02	4
Euro OTC	Sodium citrate	15111017-01	1
Euro OTC	Sodium citrate	1311025-01	1
Euro OTC	Sodium citrate	1107011-02	1
Euro OTC	Sodium citrate	1710006-015607	1
Euro OTC	Sodium citrate	48(08598497)	1
Euro OTC	Sodium citrate	2114M1900	1
Euro OTC	Sodium citrate	3048768	2
Euro OTC	Sodium citrate	160740-01	1
Euro OTC	Sodium citrate	161001601	1
Euro OTC	Sodium citrate	5116E-01900	1
Euro OTC	Sodium citrate	1807035-01ciclo	1
euro//Noweda	Sodium citrate	1701029-01	1
Euro/Phönix	Sodium citrate	1305001-01	1
Euro/Phönix	Sodium citrate	1610016-01	1
Euro OTC	Sodium citrate	1305001-01	11
Euro OTC	Sodium citrate	156422	1
Euro OTC	Sodium citrate	2546426	1
Euro OTC	Sodium citrate	3454	1
Euro OTC	Sodium citrate	1645265	3
Euro OTC	Sodium citrate	358528	1
Euro OTC	Sodium citrate	815757/6745	1
Euro OTC	Sodium citrate	25425	2
Euro OTC	Sodium citrate	12345	2
Euro OTC	Sodium citrate	13I24-B13-287921	1
Euro OTC	Sodium citrate	1404033-01	12
Euro OTC	Sodium citrate	171006-02	1
Euro OTC	Sodium citrate	1901035-01	9
Euro OTC	Sodium citrate	3032981	1
Euro OTC	Sodium citrate	901035-011	1
Euro OTC	Sodium citrate	1607040-01	11
Europ Ots Pharma	Sodium citrate	13089304	1
Fagron	Sodium citrate	31051202	1
Fagron	Sodium citrate	12A05-N04	2
Fagron	Sodium citrate	3311E-01900	1
Fagron	Sodium citrate	1234567	1
Fagron	Sodium citrate	712A-01900	1
Fagron	Sodium citrate	13A07-N01	6
Fagron	Sodium citrate	1161207	3
Fagron	Sodium citrate	13B28-N02	6
Fagron	Sodium citrate	Probe	1
Fagron	Sodium citrate	24121301	1
Fagron	Sodium citrate	13089331	1
Fagron	Sodium citrate	13/24-B13-287921	3
Fagron	Sodium citrate	13A07-N01	1
Fagron	Sodium citrate	14112502	2
Fagron	Sodium citrate	14A13_b02_300395	1
Fagron	Sodium citrate	14369402	2
Fagron	Sodium citrate	13D09N01	1
Fagron	Sodium citrate	15C27-B01-312231	6
Fagron	Sodium citrate	15C27-B01-309893	4
Fagron	Sodium citrate	15c27-b01-321097	1
Fagron	Sodium citrate	15C27-B01-321097	1
Fagron	Sodium citrate	179915	2
Fagron	Sodium citrate	15C27-B01-3211097	1
Fagron	Sodium citrate	16F10-B01-327510	5
Fagron	Sodium citrate	15C27	1
Fagron	Sodium citrate	15C27-B01-323451	1
Fagron	Sodium citrate	17A26-B04-331528	14

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Supplier	Substance	Batch	Spectra
Fagron	Sodium citrate	1211142	2
Fagron	Sodium citrate	17A26-B04-332871	26
Fagron	Sodium citrate	17A26-B04-335680	24
Fagron	Sodium citrate	17H07-B04_338530	28
Fagron	Sodium citrate	17H07-B04-341746	2
Fagron	Sodium citrate	1710006-01	1
Fagron	Sodium citrate	17H07-B04	1
Fagron	Sodium citrate	17H07	1
Fagron	Sodium citrate	18C05-B03	2
Fagron	Sodium citrate	18B14-B08-348067	3
Fagron	Sodium citrate	18G25-B07	1
Fagron	Sodium citrate	1234468	1
Fagron	Sodium citrate	18G25-B07-354812	2
Fagron	Sodium citrate	13D09-N01	4
Fagron	Sodium citrate	14A13-B02-300395	4
Fagron	Sodium citrate	1172108	1
Fagron	Sodium citrate	1219546	1
Fagron	Sodium citrate	17A26-B04-331525	1
Fagron	Sodium citrate	18G25-B07-352737	1
Fagron	Sodium citrate	12339502	1
Fagron	Sodium citrate	160614	1
Fagron	Sodium citrate	1176767	3
Fagron	Sodium citrate	1190802	1
Fagron	Sodium citrate	18L13-B02-359449	2
Fagron	Sodium citrate	179915-0001	1
Fagron	Sodium citrate	15C27-B01-316106	1
Fagron	Sodium citrate	123456test	1
Fagron	Sodium citrate	16F10-B1-327510	1
Fagron	Sodium citrate	17A26-B04-332866	1
Fagron	Sodium citrate	13I24-B13-287921	2
Fagron	Sodium citrate	815Q-01900	1
Fagron	Sodium citrate	1511017-01	1
Fagron	Sodium citrate	17A26-B04-335883	2
Fagron	Sodium citrate	18B14-B08	1
Fagron	Sodium citrate	18L13B023549449	1
Fagron	Sodium citrate	18C05-B03-350564	2
fargon	Sodium citrate	100772-114-91	1
Fargon GmbH & Co.KG	Sodium citrate	16F10-B01-326088	1
Fargon/Alliance HC	Sodium citrate	13/24-B13-287921	1
Fiebig	Sodium citrate	12J26-N02	1
Fiebig	Sodium citrate	1607002-01	2
Fiebig	Sodium citrate	1610016-01	1
Gatt-Koller	Sodium citrate	1073/04121412	1
Gehe	Sodium citrate	12045026	1
Gehe	Sodium citrate	1311035-01	1
Gehe	Sodium citrate	18G25-B07	1
Gehe	Sodium citrate	1901035-01	2
Gehe	Sodium citrate	18B14-B08-348067	1
Gehe	Sodium citrate	18L13-B02-359449	1
GEHE	Sodium citrate	17A26-B04-332866	5
GEHE	Sodium citrate	17A26-B04-331525	6
GEHE	Sodium citrate	1710006-02	1
GEHE	Sodium citrate	17H507-A04-347340	1
Euro OTC	Sodium citrate	1107011-01	1
Gehe 26.05.2014	Sodium citrate	13B28-N02	1
Gehe/Euro	Sodium citrate	1412014-01	6
Gehe/Euro	Sodium citrate	1404033-01	2
Kehr	Sodium citrate	17A26-B04-331525	1
Euro OTC	Sodium citrate	1610016-01	32
L12	Sodium citrate	16217905	1

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continued from previous page

Supplier	Substance	Batch	Spectra
L12	Sodium citrate	17323608	1
Nachprüfung	Sodium citrate	1205026-02	1
Nachprüfung 31.12.2018	Sodium citrate	14112517	2
Noweda	Sodium citrate	11127001	1
Noweda	Sodium citrate	12045026	1
Noweda	Sodium citrate	14A13-B02-294541	1
Noweda	Sodium citrate	1511017-01	1
Noweda	Sodium citrate	16095707	1
Noweda	Sodium citrate	1701029-01	1
Noweda	Sodium citrate	1710006-01	1
Noweda	Sodium citrate	17H07-B04-341746	1
Noweda	Sodium citrate	3032981	1
Noweda	Sodium citrate	17H07-B04	1
Noweda	Sodium citrate	17H07-B04-345098	1
Caelo	Sodium citrate	1511017-01	3
Euro OTC	Sodium citrate	1412014-01	15
Nowedan 15.11.2019	Sodium citrate	1909020-01	1
Euro OTC	Sodium citrate	30111301	1
Euro OTC	Sodium citrate	1521017-01	1
Phoenix	Sodium citrate	1511017-01	2
Phoenix	Sodium citrate	1506041-01	1
Phoenix	Sodium citrate	1710006-02	1
Phoenix	Sodium citrate	1901035-01	2
Phoenix	Sodium citrate	3422	1
Phoenix 30.05.2016	Sodium citrate	14369423	1
Phönix	Sodium citrate	1205026-02	1
Phönix	Sodium citrate	12045019	1
Phönix	Sodium citrate	12045024	1
Phönix	Sodium citrate	1807035-01	1
Phönix	Sodium citrate	1807035-02	1
Caelo	Sodium citrate	17323608	21
Euro OTC	Sodium citrate	180735-01	1
Sanacoro W.E:15.05.14 ...	Sodium citrate	14112502	1
Sanacorp	Sodium citrate	13089308	1
Sanacorp	Sodium citrate	13089331	1
Sanacorp	Sodium citrate	1311035-01	1
Sanacorp	Sodium citrate	1436407	1
Sanacorp	Sodium citrate	17A26-B04-332866	1
Caelo	Sodium citrate	8/AKD41	1
Fagron	Sodium citrate	12I10-N01	1
Test	Sodium citrate	1234	1
Unisan	Sodium citrate	S/WReferenzUmstell	1
Unisan	Sodium citrate	1701029-01	1
VDL;16.05.15;3,83EUR	Sodium citrate	14369406	1
Caelo	Sodium citrate	12045026	7
Caelo	Sodium citrate		8
Caelo	Sodium citrate	13089335	7
Caelo	Sodium citrate	14112517	10
Euro OTC	Sodium citrate		4
Fagron	Sodium citrate	14A13-B02-294541	8
Fagron	Sodium citrate	12E04-N05	1
Fagron	Sodium citrate	16F10-B01-326088	2
HiperScan	Sodium citrate		1
Test	Sodium citrate		1

- 110 158 spectra from 741 *Apo-Ident* customers from a total of 31 641 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium citrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium citrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	500	0	110 189
Type B	0	520	0	118 622
Type C	0	1088	1	110 158

The substance/substance group *Sodium citrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8462 %)
Type C	100.0000 % (> 99.8899 %)	99.9082 % (> 99.6327 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium citrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Arginine hydrochloride	23.63	—
Gentamicin sulfate	32.63	64.99
Magnesium citrate	47.36	—
Levothyroxin sodium	47.85	—
⋮	⋮	⋮
Beclometasone dipropionate	>50	274.97
Clobetasol propionate	>50	310.02
Betamethasone dipropionate, micronized	>50	322.71
Oxybutynin hydrochloride	>50	331.64
Sodium benzoate	>50	1122.85

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium citrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20662	21839	3.89	36.22
21839	21839	0.00	38.40
22843	21997	5.50	37.96
21778	21670	3.69	34.92
20918	21670	4.32	33.55
21997	21997	0.00	38.66
22859	22859	0.00	26.75
22996	22996	0.00	37.37
21670	21670	0.00	32.63
21718	21670	2.81	34.03

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium cromoglicate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20775-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium cromoglicate; Cromolyn sodium; Natrii cromoglicas

Special notes

When selecting the *Sodium cromoglicate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium cromoglicate	8	6	6

Second-stage model

For differentiation of the substance/substance group *Sodium cromoglicate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium cromoglicate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium cromoglic...	11114501	20776	80	20110518
Caelo	Sodium cromoglic...	13232802	21375	20	1505352
Caelo	Sodium cromoglic...	13232802	21376	110	20130905
Caelo	Sodium cromoglic...	15224404	21990	60	20150625
Euro OTC	Sodium cromoglic...	1403017-01	21981	60	20140505
Euro OTC	Sodium cromoglic...	1510018	22231	60	20151109*
Euro OTC	Sodium cromoglic...	1703027	23383	40	20170405*
Fagron	Sodium cromoglic...	12C09-N02	20775	79	1401553
Fagron	Sodium cromoglic...	13G24-N04	21260	40	20130515

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 549 spectra of 9 reference samples from the substance/substance group *Sodium cromoglicate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 140 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 450 spectra of 10 reference samples from the substance/substance group *Sodium cromoglicate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium cromoglicate	173081	23855	30
Caelo	Sodium cromoglicate	182657	24382	40
Euro OTC	Sodium cromoglicate	1112003-01	20778	40
Euro OTC	Sodium cromoglicate	1711024	23871	40
Euro OTC	Sodium cromoglicate	1811016	24424	40
Fagron	Sodium cromoglicate	15C23-B01-307751	22972	40
Caelo	Sodium cromoglicate	15224404	21990SI [†]	60
Euro OTC	Sodium cromoglicate	1403017-01	21981SI [†]	60
Euro OTC	Sodium cromoglicate	1510018	22231SI [†]	60
Fagron	Sodium cromoglicate	15C23-B01-307751	22972SI	40

- 118 692 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH, Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 10 *Apo-Ident* customers from 9 batches from the substance/substance group *Sodium cromoglicate*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Sodium cromoglicate	15414502	1
Caelo	Sodium cromoglicate	16270705	2
Caelo	Sodium cromoglicate	12301102	1
Caelo	Sodium cromoglicate	5113A-02831	1
E Plus	Sodium cromoglicate	15414502	1
Euro OTC	Sodium cromoglicate	170302701	1
Fagron	Sodium cromoglicate	13E22-N11	1
Caelo	Sodium cromoglicate	15224404	1
Euro OTC	Sodium cromoglicate	1403017-01	1
Fagron	Sodium cromoglicate	13G24-N04	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 882 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Validation results

The validation runs checked whether the substance/substance group *Sodium cromoglicate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium cromoglicate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	501	48	110 140
Type B	0	440	10	118 692
Type C	0	10	1	111 236

The substance/substance group *Sodium cromoglicate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	91.2568 % (> 90.7104 %)
Type B	100.0000 % (> 99.9893 %)	97.7778 % (> 97.1111 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium cromoglicate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	36.02	—
Chloramphenicol	46.39	—
Levothyroxin sodium	59.75	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium cromoglicate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20775	20775	0.00	67.52
20776	20775	15.24	75.88
21260	22231	7.66	68.90
21376	21375	4.38	63.88
21981	20775	15.63	80.43
21990	20775	14.43	82.61
22231	22231	0.00	74.03
23383	23383	0.00	72.33
21375	21375	0.00	73.83

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium cyclamate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20917-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium cyclamate; Natrii cyclamas

Special notes

When selecting the *Sodium cyclamate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium cyclamate	3	2	20

Second-stage model

For differentiation of the substance/substance group *Sodium cyclamate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium cyclamate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium cyclamate	12256803	20917	40	1401418
Caelo	Sodium cyclamate	12105622	21380	40	20120423
Caelo	Sodium cyclamate	182167	24379	40	20181023*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Sodium cyclamate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Sodium cyclamate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium cyclamate	16119302	23259	40
Caelo	Sodium cyclamate	170411	23853	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 52 spectra from 45 *Apo-Ident* customers from 21 batches from the substance/substance group *Sodium cyclamate*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium cyclamate	10380915	2
Caelo	Sodium cyclamate	11204205	1
Caelo	Sodium cyclamate	15201608	3
Caelo	Sodium cyclamate	15201614	1
Caelo	Sodium cyclamate	16119302	4
Caelo	Sodium cyclamate	16119310	1
Caelo	Sodium cyclamate	18216702	4
Caelo	Sodium cyclamate	18216707	1
Caelo	Sodium cyclamate	179617362207	1
Caelo	Sodium cyclamate	14149602	1
Caelo	Sodium cyclamate	17362207	2
Caelo	Sodium cyclamate	17362208	1
Caelo	Sodium cyclamate	15201606	2
Caelo	Sodium cyclamate	15201601	2
Caelo	Sodium cyclamate	16119308	4
Caelo	Sodium cyclamate	17362202	7
Caelo	Sodium cyclamate	18216704	1
Caelo	Sodium cyclamate	17041102	7
Caesar & Loretz GmbH	Sodium cyclamate	12105622	1
Caesar & Loretz GmbH	Sodium cyclamate	18216702	1
Caesar & Loretz GmbH	Sodium cyclamate	17362208	1
Caesar&Loretz GmbH/ San...	Sodium cyclamate	16119308	1
Euro OTC	Sodium cyclamate	16119302	1
Phoenix	Sodium cyclamate	787/03100611	1
Caelo	Sodium cyclamate	16119302/2280217	1

- 111 195 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium cyclamate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium cyclamate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	80	0	119 062
Type C	0	46	6	111 195

The substance/substance group *Sodium cyclamate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	88.4615 % (> 82.6923 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium cyclamate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Biotin	57.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium cyclamate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20917	20917	0.00	53.26
21380	20917	12.21	53.46
24379	24379	0.00	54.70

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium edetate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20937-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium edetate; Dinatrii edetas

Special notes

When selecting the *Sodium edetate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium edetate	6	7	120

Second-stage model

For differentiation of the substance/substance group *Sodium edetate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium edetate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium edetate	13142009	21362	40	20130524
Caelo	Sodium edetate	161364	22465	60	20160504*
Euro OTC	Sodium edetate	1609023	22915	40	20170106*
Euro OTC	Sodium edetate	1812016	24414	40	20190116*
Fagron	Sodium edetate	13E15-N05	20937	40	1402193
Fagron	Sodium edetate	16F21-B02-325085	22926	40	20160713

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Sodium edetate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 429 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 8 reference samples from the substance/substance group *Sodium edetate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium edetate	172618	23663	40
Euro OTC	Sodium edetate	1609023-01	22950	40
Euro OTC	Sodium edetate	1704011	23390	40
Euro OTC	Sodium edetate	1806007	24157	40
Euro OTC	Sodium edetate	1807025	24159	40
Euro OTC	Sodium edetate	1901032	24472	40
Euro OTC	Sodium edetate	1909030	24958	40
Caelo	Sodium edetate	172618	23818	40

- 118 822 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 445 spectra from 265 *Apo-Ident* customers from 129 batches from the substance/substance group *Sodium edetate*.
- Among them are spectra of independent samples from 120 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium edetate	13E15-N05	1
Fagron	Sodium edetate	14G03-B05_307737	1
Alliance Healthcare	Sodium edetate	12181714	1
Alliance Healthcare	Sodium edetate	13E15-N05	2
Anzag	Sodium edetate	13K19-B02-290051	1
Bombastus	Sodium edetate	16136404	1
Caelo	Sodium edetate	15427710	5
Caelo	Sodium edetate	3211I-01925	1
Caelo	Sodium edetate	12E16-N04	1
Caelo	Sodium edetate	12181704	1
Caelo	Sodium edetate	92159379	1
Caelo	Sodium edetate	12254507	2
Caelo	Sodium edetate	2913M1925	1
Caelo	Sodium edetate	13E15-N05	4
Caelo	Sodium edetate	13142004	4
Caelo	Sodium edetate	13142008	6
Caelo	Sodium edetate	13142014	1
Caelo	Sodium edetate	13142010	2
Caelo	Sodium edetate	2101414	1
Caelo	Sodium edetate	13K19-B02-290051	1
Caelo	Sodium edetate	13395002	3
Caelo	Sodium edetate	13395007	4
Caelo	Sodium edetate	14270506	4
Caelo	Sodium edetate	15116602	4
Caelo	Sodium edetate	14G03-B05-307737	1
Caelo	Sodium edetate	15427705	4
Caelo	Sodium edetate	15427714	22
Caelo	Sodium edetate	1517E-01925	1
Caelo	Sodium edetate	16337302	6
Caelo	Sodium edetate	17336102	13

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Supplier	Substance	Batch	Spectra
Caelo	Sodium edetate	14031801	1
Caelo	Sodium edetate	17d25-b08-339881	1
Caelo	Sodium edetate	17D25-B08-343253	1
Caelo	Sodium edetate	18H03-B04	1
Caelo	Sodium edetate	18007112	1
Caelo	Sodium edetate	10887102	1
Caelo	Sodium edetate	12181702	1
Caelo	Sodium edetate	15116603	14
Caelo	Sodium edetate	12181703	3
Caelo	Sodium edetate	11074608	2
Caelo	Sodium edetate	15035603	2
Caelo	Sodium edetate	15035604	4
Caelo	Sodium edetate	15427704	4
Caelo	Sodium edetate	13142018	2
Caelo	Sodium edetate	12181711	12
Caelo	Sodium edetate	14270505	2
Caelo	Sodium edetate	17336115	1
Caelo	Sodium edetate	12181714	4
Caelo	Sodium edetate	12181706	2
Caelo	Sodium edetate	16337312	17
Caelo	Sodium edetate	16337316	6
Caelo	Sodium edetate	18007102	5
Caelo	Sodium edetate	13142002	4
Caelo	Sodium edetate	1427006	1
Caelo	Sodium edetate	15427703	14
Caelo	Sodium edetate	18007110	6
Caelo	Sodium edetate	3913A-01925	1
Caelo	Sodium edetate	15427717	8
Caelo	Sodium edetate	18H03-B04-357771	1
Caelo	Sodium edetate	13/23-N03-3472312131	1
Caelo	Sodium edetate	16136404	5
Caesar & Loretz GmbH	Sodium edetate	13142008	1
Caesar & Loretz GmbH	Sodium edetate	14270505	1
Caesar & Loretz GmbH	Sodium edetate	15427705	1
Caesar & Loretz GmbH	Sodium edetate	16337312	1
Caesar & Loretz GmbH / ...	Sodium edetate	13142004	1
Caesar & Loretz GmbH, 4...	Sodium edetate	12181711	1
Cranach-Apotheke	Sodium edetate	11a31-no6	1
Delta Apotheke	Sodium edetate	18007102	2
Euro OTC	Sodium edetate	13142018	1
Euro OTC	Sodium edetate	15427703	1
Euro OTC	Sodium edetate	16337312	1
Fagron	Sodium edetate	12E16-N04	2
Fagron	Sodium edetate	813Q-01925	1
Fagron	Sodium edetate	12E12-N04	1
Fagron	Sodium edetate	12G25-N12	3
Fagron	Sodium edetate	601HA062	6
Fagron	Sodium edetate	13I23-N03	10
Fagron	Sodium edetate	13G15-N03	4
Fagron	Sodium edetate	13K19-B02-289035	1
Fagron	Sodium edetate	13E15-B10-289034	1
Fagron	Sodium edetate	13K19-B02-290051	10
Fagron	Sodium edetate	14G03-B05-30773	1
Fagron	Sodium edetate	13k19-b02-290051	2
Fagron	Sodium edetate	11A31-N06Retest	1
Fagron	Sodium edetate	14G03B05309971	1
Fagron	Sodium edetate	14G03-B05-309971	1
Fagron	Sodium edetate	14G03-B05-307737	6
Fagron	Sodium edetate	15D01-B05-315877	2
Fagron	Sodium edetate	16F21-B02-324370	3

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Supplier	Substance	Batch	Spectra
Fagron	Sodium edetate	16F21-B02-325891	2
Fagron	Sodium edetate	11A31-N06	1
Fagron	Sodium edetate	16F21-B02	3
Fagron	Sodium edetate	16F21-B02-329900	1
Fagron	Sodium edetate	16F21-B02-332039	1
Fagron	Sodium edetate	16F21-B02-333607	1
Fagron	Sodium edetate	17D25-B08-338202	1
Fagron	Sodium edetate	601H9118	1
Fagron	Sodium edetate	17D25-B08-339881	3
Fagron	Sodium edetate	17D25-B08-343253	1
Fagron	Sodium edetate	18H03-B04-355280	6
Fagron	Sodium edetate	18h03-b04-356574	1
Fagron	Sodium edetate	14G03-B05-303420	1
Fagron	Sodium edetate	17D25-B08-336718	2
Fagron	Sodium edetate	18H03-B04-357771	1
Fagron	Sodium edetate	16F21B02327696	1
Fagron	Sodium edetate	601H1300	2
Fagron	Sodium edetate	18H03-B04	1
Fagron	Sodium edetate	16f21-b02-327696	1
Fagron	Sodium edetate	13I23-N03	1
Fagron	Sodium edetate	17D25-B08-334827	1
Fagron	Sodium edetate	18H03-B04-353034	4
Fagron	Sodium edetate	13/23-N03	6
Fagron	Sodium edetate	13K19-B02-290052	3
Fagron	Sodium edetate	14G03-B05	5
Fagron	Sodium edetate	17D25B08343253	1
Fagron	Sodium edetate	12g25-n12	1
Fagron	Sodium edetate	601EE047	2
Fagron	Sodium edetate	13K19-B02	1
Fagron	Sodium edetate	16F21-B02-327696	5
Fagron	Sodium edetate	601EC350	1
Fagron	Sodium edetate	17D25-Bo8-336718	1
Fagron	Sodium edetate	13K19B02	1
Fagron	Sodium edetate	601EB174	1
Fagron	Sodium edetate	17D25-B08-334827	4
Fagron	Sodium edetate	13K19B02290051	1
Fagron	Sodium edetate	601EB262	1
Fagron	Sodium edetate	15D01-B05-317369	1
Fagron	Sodium edetate	17D25-B08	3
Fagron	Sodium edetate	5012Q-01925	1
Fagron	Sodium edetate	914E-01925	1
Fagron	Sodium edetate	215I-01925	1
Fagron	Sodium edetate	5315A-01925	1
Fagron	Sodium edetate	16F21-B02-323074	1
Fargon	Sodium edetate	18H03-B04	1
Fargon	Sodium edetate	18H03-B04-353034	1
Fargron / Noweda	Sodium edetate	16f21-b0-330959	1
Fiebig	Sodium edetate	16F21-B02-327696	1
Fiebig	Sodium edetate	18007110	1
Gehe	Sodium edetate	13E15-N05	1
Gehe	Sodium edetate	13142018	1
kehr	Sodium edetate	17D25-B08-339881	1
Caelo	Sodium edetate	16F21-B02-327696	1
Noweda	Sodium edetate	601H1300	1
Noweda	Sodium edetate	15427710	1
Noweda	Sodium edetate	16337312	1
Fagron	Sodium edetate	164599-0001	1
Fagron	Sodium edetate	16f21-b02-330959	1
Noweda/Gehe	Sodium edetate	14G03-B05-307737	1
Phoenix	Sodium edetate	15427704	1

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Supplier	Substance	Batch	Spectra
Phoenix	Sodium edetate	16F21-B02-333607	1
Phoenix	Sodium edetate	18007110	1
Phoenix	Sodium edetate	3411	1
Phoenix Goettin	Sodium edetate	13G15-N03	1
Phoenix Goettin	Sodium edetate	13G15-N03	1
Caelo	Sodium edetate	13142015	4
phönix	Sodium edetate	13142018	1
phönix	Sodium edetate	13K19-B02-290051	1
phönix	Sodium edetate	15427703	1
phönix	Sodium edetate	15427704	1
Phönix	Sodium edetate	11074702	1
Phönix	Sodium edetate	13142004	1
Phönix	Sodium edetate	13G15-N03	1
Phönix	Sodium edetate	13E15-B10	1
Phönix	Sodium edetate	16F21-B02-327696	1
Phönix	Sodium edetate	164599-0001	1
sanacorp	Sodium edetate	16F21-B02-324370	1
Sanacorp	Sodium edetate	12G25-N12	2
Sanacorp	Sodium edetate	6/AKD14	1
Sanacorp	Sodium edetate	13E15-N05	1
Sanacorp	Sodium edetate	1505603	1
Caelo	Sodium edetate	11074703	1
	Sodium edetate	13142009	1
Bombastus	Sodium edetate		1
Caelo	Sodium edetate	13142009	9
Caelo	Sodium edetate		1
Fagron	Sodium edetate	13E15-N05	9
Fagron	Sodium edetate	16F21-B02-325085	6

- 110 802 spectra from 742 *Apo-Ident* customers from a total of 31 763 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium edetate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium edetate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	320	0	118 822
Type C	0	442	3	110 802

The substance/substance group *Sodium edetate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 99.8899 %)	99.3258 % (> 98.6517 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium edetate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	64.81	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium edetate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22926	22465	3.80	77.92
20937	20937	0.00	78.85
21362	22465	2.83	78.51
22465	22465	0.00	78.93
22915	22915	0.00	80.96
24414	24414	0.00	71.98

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium methyl-4-hydroxybenzoate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 22602-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium methyl-4-hydroxybenzoate; Methylis parahydroxybenzoas natricus

Special notes

When selecting the *Sodium methyl-4-hydroxybenzoate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium methyl-4-hydroxybenzoate	4	1	2

Second-stage model

For differentiation of the substance/substance group *Sodium methyl-4-hydroxybenzoate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium methyl-4-hydroxybenzoate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium methyl-4-...	15358708	22602	40	AR-16-FG-015095-01
Caelo	Sodium methyl-4-...	15358708	22603	40	20151127
Caelo	Sodium methyl-4-...	15358713	23093	40	20151127
Caelo	Sodium methyl-4-...	170519	23289	40	20170308*
Caelo	Sodium methyl-4-...	191439	24726	40	20190628*

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 5 reference samples from the substance/substance group *Sodium methyl-4-hydroxybenzoate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110489 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Sodium methyl-4-hydroxybenzoate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium methyl-4-hydroxybenzo...	15358709	22776	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Sodium methyl-4-hydroxybenzoate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium methyl-4-hydroxybenzo...	17051903	1
Caelo	Sodium methyl-4-hydroxybenzo...	18060801	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium methyl-4-hydroxybenzoate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium methyl-4-hydroxybenzoate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	40	0	119 102
Type C	0	2	0	111 245

The substance/substance group *Sodium methyl-4-hydroxybenzoate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium methyl-4-hydroxybenzoate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dithranol	53.29	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium methyl-4-hydroxybenzoate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24726	24726	0.00	71.05
22602	22602	0.00	72.03
22603	22602	2.74	72.77
23093	22602	5.03	74.30
23289	23289	0.00	77.29

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium salicylate, powdered**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21037-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium salicylate, powdered; Natrii salicylas plv.

Special notes

When selecting the *Sodium salicylate, powdered* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium salicylate, powdered	3	1	5

Second-stage model

For differentiation of the substance/substance group *Sodium salicylate, powdered* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium salicylate, powdered*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium salicylat...	12158307	21037	40	1403225
Caelo	Sodium salicylat...	13140513	21689	60	20130531
Caelo	Sodium salicylat...	163053	23052	40	20161118*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Sodium salicylate, powdered*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Sodium salicylate, powdered*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sodium salicylate, powdered	16305301	22879	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 5 spectra from 4 *Apo-Ident* customers from 5 batches from the substance/substance group *Sodium salicylate, powdered*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sodium salicylate, powdered	18061305	1
Fagron	Sodium salicylate, powdered	102091210	1
GATT-KOLLER/PHOENIX	Sodium salicylate, powdered	4853/11124512	1
Gehe	Sodium salicylate, powdered	13G31-B03-287961	1
Phoenix	Sodium salicylate, powdered	12158309	1

- 111 242 spectra from 742 *Apo-Ident* customers from a total of 31 886 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium salicylate, powdered* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium salicylate, powdered* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	40	0	119 102
Type C	0	4	1	111 242

The substance/substance group *Sodium salicylate, powdered* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8901 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium salicylate, powdered* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-tryptophan	67.75	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium salicylate, powdered* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21037	21037	0.00	67.72
21689	21037	3.85	68.51
23052	23052	0.00	65.91

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sodium tetraborate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20179-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sodium tetraborate; Borax

Special notes

When selecting the *Sodium tetraborate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sodium tetraborate	6	4	21

Second-stage model

For differentiation of the substance/substance group *Sodium tetraborate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sodium tetraborate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sodium tetraborate	13290118	21438	60	1412042
Caelo	Sodium tetraborate	161372	22475	60	20160624*
Caelo	Sodium tetraborate	161372	22621	40	20160624*
Euro OTC	Sodium tetraborate	1404025-01	21656	60	20140514
Euro OTC	Sodium tetraborate	1507024	21854	60	20150730*
Euro OTC	Sodium tetraborate	1510032	22235	60	20151118*
Euro OTC	Sodium tetraborate	1711002	23892	40	20171128*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 7 reference samples from the substance/substance group *Sodium tetraborate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 309 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Sodium tetraborate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Sodium tetraborate	1603043	22508	40
Euro OTC	Sodium tetraborate	1607036	22713	40
Euro OTC	Sodium tetraborate	1701046	22990	40
Euro OTC	Sodium tetraborate	1804014	24093	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 35 spectra from 26 *Apo-Ident* customers from 23 batches from the substance/substance group *Sodium tetraborate*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Borax Francais	Sodium tetraborate	1402002-01	1
Caelo	Sodium tetraborate	11369431	1
Caelo	Sodium tetraborate	21051402	1
Caelo	Sodium tetraborate	14310905	2
Caelo	Sodium tetraborate	16137201	1
Caelo	Sodium tetraborate	16081801	1
Caelo	Sodium tetraborate	1309032-01	1
Caelo	Sodium tetraborate	1607036-01	1
EuRho	Sodium tetraborate	1607036-01	2
Euro OTC	Sodium tetraborate	13111207	1
Euro OTC	Sodium tetraborate	1507024-01	3
Euro OTC	Sodium tetraborate	1607036-01	1
Euro OTC	Sodium tetraborate	1711002-01	5
Euro OTC	Sodium tetraborate	160304301	1
Euro OTC	Sodium tetraborate	1701046-01	1
Euro OTC	Sodium tetraborate	1503043-01	1
Euro OTC	Sodium tetraborate	1408006-01	1
Euro OTC	Sodium tetraborate	1302034-01	1
Euro OTC	Sodium tetraborate	130203401	1
Euro/Alliance Healthcare	Sodium tetraborate	171100201	1
Euro OTC	Sodium tetraborate	1309032-01	1
Fagron	Sodium tetraborate	12H09-N03	1
Gatt-Koller / Phoenix	Sodium tetraborate	6187/01142114	1
Phoenix	Sodium tetraborate	1603043-01	1
Sanacorp	Sodium tetraborate	171100201	1
Caelo	Sodium tetraborate	13290118	1
Euro OTC	Sodium tetraborate		1

- 111 212 spectra from 742 *Apo-Ident* customers from a total of 31 869 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sodium tetraborate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sodium tetraborate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	367	13	110 309
Type B	0	158	2	118 982
Type C	0	35	0	111 212

The substance/substance group *Sodium tetraborate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	96.5789 % (> 95.7895 %)
Type B	100.0000 % (> 99.9893 %)	98.7500 % (> 96.8750 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 82.8571 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sodium tetraborate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	27.06	—
Oxytetracycline hydrochloride	46.68	—
Magnesium citrate	48.53	—
Oxalic acid	60.27	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sodium tetraborate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22621	22621	0.00	42.22
23892	23892	0.00	30.31
21438	21438	0.00	43.33
21656	22475	5.86	45.58
21854	21854	0.00	39.35
22235	22235	0.00	38.42
22475	22475	0.00	43.66

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sorbic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20881-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sorbic acid; Acidum sorbicum

Special notes

When selecting the *Sorbic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sorbic acid	8	1	62

Second-stage model

For differentiation of the substance/substance group *Sorbic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sorbic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sorbic acid	12038025	20881	40	20120315
Caelo	Sorbic acid	13334008	21460	60	AR-15-FG-007849-01
Caelo	Sorbic acid	14176214	22592	40	20140708
Caelo	Sorbic acid	14380714	22593	40	20150209
Caelo	Sorbic acid	162080	22616	40	20160722*
Caelo	Sorbic acid	15382002	22826	40	20151112
Caelo	Sorbic acid	172056	23851	40	20170823*
Caelo	Sorbic acid	162080	23859	40	20160722*
Caelo	Sorbic acid	191114	24569	40	20190502*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 380 spectra of 9 reference samples from the substance/substance group *Sorbic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 309 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Sorbic acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sorbic acid	182876	24384	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 346 spectra from 235 *Apo-Ident* customers from 69 batches from the substance/substance group *Sorbic acid*.
- Among them are spectra of independent samples from 62 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ALH	Sorbic acid	15382007	1
Anzag	Sorbic acid	12038016	1
Caelo	Sorbic acid	29071201	1
Caelo	Sorbic acid	10305209	1
Caelo	Sorbic acid	5012E-01048	1
Caelo	Sorbic acid	12038002	1
Caelo	Sorbic acid	12038020	4
Caelo	Sorbic acid	10305208	1
Caelo	Sorbic acid	10120303	1
Caelo	Sorbic acid	105505	1
Caelo	Sorbic acid	13334003	4
Caelo	Sorbic acid	13334010	7
Caelo	Sorbic acid	14176206	7
Caelo	Sorbic acid	14176209	5
Caelo	Sorbic acid	14176207	1
Caelo	Sorbic acid	14176212	7
Caelo	Sorbic acid	14380702	3
Caelo	Sorbic acid	14380715	1
Caelo	Sorbic acid	15382001	1
Caelo	Sorbic acid	15382007	4
Caelo	Sorbic acid	15382010	13
Caelo	Sorbic acid	28041726	1
Caelo	Sorbic acid	16208009	11
Caelo	Sorbic acid	16208011	12
Caelo	Sorbic acid	16208015	9
Caelo	Sorbic acid	16208016	10
Caelo	Sorbic acid	16208018	2
Caelo	Sorbic acid	21041801	1
Caelo	Sorbic acid	17343411	16
Caelo	Sorbic acid	17343422	8
Caelo	Sorbic acid	1827669	1
Caelo	Sorbic acid	18284605	1

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Supplier	Substance	Batch	Spectra
Caelo	Sorbic acid	18287605	10
Caelo	Sorbic acid	4811Q-01048	1
Caelo	Sorbic acid	11203807	10
Caelo	Sorbic acid	9280207	1
Caelo	Sorbic acid	12330618	12
Caelo	Sorbic acid	16208007	1
Caelo	Sorbic acid	12330608	8
Caelo	Sorbic acid	18287616	6
Caelo	Sorbic acid	1620808005	1
Caelo	Sorbic acid	17343401	6
Caelo	Sorbic acid	16208012	8
Caelo	Sorbic acid	12038016	6
Caelo	Sorbic acid	170427AS/16208005	1
Caelo	Sorbic acid	16208020	10
Caelo	Sorbic acid	18287609	9
Caelo	Sorbic acid	12038012	1
Caelo	Sorbic acid	14380706	5
Caelo	Sorbic acid	16208005	25
Caelo	Sorbic acid	11203806	2
Caelo	Sorbic acid	162508016	1
Caelo	Sorbic acid	14176213	1
Caelo	Sorbic acid	11203812	1
Caelo	Sorbic acid	12038009	1
Caelo	Sorbic acid	14380704	1
Caelo	Sorbic acid	14380713	2
Caelo	Sorbic acid	15123912	1
Caelo / Phoenix	Sorbic acid	18287616	1
Caesar & Loretz GmbH	Sorbic acid	18287605	2
Caesar & Loretz GmbH / ...	Sorbic acid	16208009	1
Caesar & Loretz/Noweda	Sorbic acid	14380706	1
Euro OTC	Sorbic acid	o216E-01048	1
Euro OTC	Sorbic acid	12038020	1
Fagron	Sorbic acid	13334008	1
Fagron	Sorbic acid	14176206	1
Fagron	Sorbic acid	121394	1
Fagron	Sorbic acid	17343422	1
Fiebig	Sorbic acid	168009	1
Finze	Sorbic acid	9280207	1
Fischar	Sorbic acid	16208005	1
Gatt-Koller / Phoenix	Sorbic acid	2575/07142914	1
Gehe	Sorbic acid	16208011	1
Gehe	Sorbic acid	17343401	1
Gehe	Sorbic acid	18287609	1
GEHE	Sorbic acid	17343401	1
Th. Geyer	Sorbic acid	17343411	1
H.Lamotte	Sorbic acid	17343401	1
L12	Sorbic acid	15382010	1
L12	Sorbic acid	18287602	1
Noweda	Sorbic acid	12038016	1
Noweda	Sorbic acid	12330608	1
Noweda	Sorbic acid	14176206	1
Noweda	Sorbic acid	14380706	1
Noweda	Sorbic acid	18287605	1
Phoenix	Sorbic acid	11203813	1
Phoenix 17.4.13	Sorbic acid	12038020	1
PHOENIX 12.05.2014	Sorbic acid	13334008	1
phönix	Sorbic acid	15382010	1
Phönix	Sorbic acid	12330618	1
Phönix	Sorbic acid	16208005	1
Phönix	Sorbic acid	18287605	1

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Supplier	Substance	Batch	Spectra
Sanacorp	Sorbic acid	12038016	1
Sanacorp	Sorbic acid	13334008	1
SanacorpWE: 23.09.14 E...	Sorbic acid	14176212	1
VDL;5,78EUR;18.12	Sorbic acid	14176206	1
Caelo	Sorbic acid	14176214	11
Caelo	Sorbic acid	13334008	5
Caelo	Sorbic acid	14380714	9
Caelo	Sorbic acid	15382002	10
Caelo	Sorbic acid	162080	1
Caelo	Sorbic acid	12038025	1
vdl 28.04.2014 preis:5,79	Sorbic acid		1

- 110 901 spectra from 742 *Apo-Ident* customers from a total of 31 824 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sorbic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sorbic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	380	0	110 309
Type B	0	40	0	119 102
Type C	0	332	14	110 901

The substance/substance group *Sorbic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	95.9538 % (> 95.0867 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sorbic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sildenafil citrate	42.08	—
Ornithine aspartate	49.87	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sorbic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20881	23851	2.71	54.81
21460	21460	0.00	53.21
22592	23851	1.75	53.56
22593	23859	2.86	54.52
22616	22616	0.00	55.07
22826	24569	2.78	52.15
23851	23851	0.00	53.62
23859	23859	0.00	53.78
24569	24569	0.00	53.12

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sorbitol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20075-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sorbitol; Sorbitolum

Special notes

When selecting the *Sorbitol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sorbitol	8	4	105

Second-stage model

For differentiation of the substance/substance group *Sorbitol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sorbitol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sorbitol	13278217	21485	40	20130920
Caelo	Sorbitol	16038501	22847	40	20160315
Caelo	Sorbitol	163531	23028	40	20170119*
Caelo	Sorbitol	16353107	23442	40	20170119
Euro OTC	Sorbitol	1506052	21834	60	20150713*
Euro OTC	Sorbitol	1512016	22293	60	20160113*
Euro OTC	Sorbitol	1604007	22539	40	20160428*
Euro OTC	Sorbitol	1610018	22849	40	20161121*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Sorbitol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 329 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Sorbitol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sorbitol	181636	24220	40
Caelo	Sorbitol	190173	24562	40
Caelo	Sorbitol	192579	24898	40
Euro OTC	Sorbitol	1810010	24306	40

- 118 982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 227 spectra from 93 *Apo-Ident* customers from 109 batches from the substance/substance group *Sorbitol*.
- Among them are spectra of independent samples from 105 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Bombastus	Sorbitol	13278206	2
Caelo	Sorbitol	13278239	1
Caelo	Sorbitol	23071201	1
Caelo	Sorbitol	12345	1
Caelo	Sorbitol	17011305	1
Caelo	Sorbitol	11379337	2
Caelo	Sorbitol	5021307	1
Caelo	Sorbitol	1083330	1
Caelo	Sorbitol	11379322	1
Caelo	Sorbitol	12249109	2
Caelo	Sorbitol	12249110	4
Caelo	Sorbitol	11379336	2
Caelo	Sorbitol	12249124	2
Caelo	Sorbitol	12249126	2
Caelo	Sorbitol	16101303	1
Caelo	Sorbitol	13335307	3
Caelo	Sorbitol	13278204	1
Caelo	Sorbitol	13278216	2
Caelo	Sorbitol	26071402	1
Caelo	Sorbitol	8081402	1
Caelo	Sorbitol	23081401	1
Caelo	Sorbitol	4091401	1
Caelo	Sorbitol	13278218	1
Caelo	Sorbitol	20021501	1
Caelo	Sorbitol	13278250	1
Caelo	Sorbitol	15208302	4
Caelo	Sorbitol	15208309	3
Caelo	Sorbitol	1512016-01	2
Caelo	Sorbitol	16038502	1

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Supplier	Substance	Batch	Spectra
Caelo	Sorbitol	15208310	4
Caelo	Sorbitol	225282222169	1
Caelo	Sorbitol	1610018-01	1
Caelo	Sorbitol	17140902	2
Caelo	Sorbitol	17366301	6
Caelo	Sorbitol	11379333	1
Caelo	Sorbitol	18163607	1
Caelo	Sorbitol	19017304	4
Caelo	Sorbitol	181636606	1
Caelo	Sorbitol	18281610	2
Caelo	Sorbitol	13278247	1
Caelo	Sorbitol	14250807	1
Caelo	Sorbitol	15118912	1
Caelo	Sorbitol	16038515	6
Caelo	Sorbitol	16038514	5
Caelo	Sorbitol	15208311	3
Caelo	Sorbitol	11379321	1
Caelo	Sorbitol	11379332	2
Caelo	Sorbitol	12249108	2
Caelo	Sorbitol	12249140	1
Caelo	Sorbitol	14250806	1
Caelo	Sorbitol	15208305	3
Caelo	Sorbitol	13278246	2
Caelo	Sorbitol	15012708	1
Caelo	Sorbitol	16353108	1
Caelo	Sorbitol	15118902	2
Caelo	Sorbitol	12L07-N12	1
Caelo	Sorbitol	18163606	4
Caelo	Sorbitol	18281605	1
Caelo	Sorbitol	10383323	1
Caelo	Sorbitol	13278241	1
Caelo	Sorbitol	15118901	3
Caelo	Sorbitol	1604007-01	1
Caelo	Sorbitol	16353102	3
Caelo	Sorbitol	17140903	6
Caelo	Sorbitol	17140904	1
Caelo	Sorbitol	15208306	2
Caelo	Sorbitol	16038503	1
Caelo	Sorbitol	133335307	1
Caelo	Sorbitol	14250808	1
Caelo	Sorbitol	15208303	1
Caelo	Sorbitol	17366304	3
Caelo	Sorbitol	12249139	1
Caelo	Sorbitol	13335304	1
Caelo	Sorbitol	13278206	1
Caelo	Sorbitol	1714090903	1
Caelo	Sorbitol	113793	1
Caesar & Loretz GmbH	Sorbitol	18163606	1
eurho	Sorbitol	1301019-01	1
EuRho	Sorbitol	161001802	1
EuRho/Anzag	Sorbitol	4712I-02298	1
Euro OTC	Sorbitol	1301019-01	3
Euro OTC	Sorbitol	1506052-01	4
Euro OTC	Sorbitol	1604007-01	4
Euro OTC	Sorbitol	1311034-01	2
Euro OTC	Sorbitol	1512016-01	3
Euro OTC	Sorbitol	1610018-01	10
Euro OTC	Sorbitol	1610018-03	5
Euro OTC	Sorbitol	1404007-01	2
Euro OTC	Sorbitol	700476	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Sorbitol	1406014-01	1
Euro OTC	Sorbitol	1501048-01	3
Euro OTC	Sorbitol	1610018-02	1
Euro OTC	Sorbitol	150652-01	1
Fagron	Sorbitol	12L17-N12	3
Fagron	Sorbitol	13E07-B40	2
Fagron	Sorbitol	13278249	1
Fagron	Sorbitol	14E21-B02	1
Fagron	Sorbitol	11I09-N11	1
Fagron	Sorbitol	12J15-N01	1
Fagron	Sorbitol	M721140	1
Fagron	Sorbitol	M721140/12L17-N12	1
Fagron	Sorbitol	13D08-N27	1
Fagron	Sorbitol	12E30-N24	3
Fagron	Sorbitol	13G04-N04	1
Gatt-Koller / Phoenix	Sorbitol	1718/0513	1
Gatt-Koller / Phoenix	Sorbitol	1718/05134013	1
Gehe	Sorbitol	18163606	1
GEHE	Sorbitol	16353108	1
GEHE	Sorbitol	19017305	1
Gehe 01.09.2014	Sorbitol	13278217	1
GEHE 28.11.2014	Sorbitol	13278245	1
L10	Sorbitol	16353108	1
L12	Sorbitol	17140904	3
Merck	Sorbitol	13D08-N27	1
Caelo	Sorbitol	13278249	1
Caelo	Sorbitol	16231208	1
Noweda/ Ichthyol	Sorbitol	1512016-01	1
Phoenix 12.08.2013	Sorbitol	12249108	1
PHÖNIX	Sorbitol	18281603	1
Sana	Sorbitol	18281603	1
Caelo	Sorbitol	11379320	1
siehe Protokoll	Sorbitol	15208310	1
Spangro 17.05.19	Sorbitol	17140902	1
Caelo	Sorbitol		1
Caelo	Sorbitol	16038501	4
Caelo	Sorbitol	16353107	1
Fagron	Sorbitol		1

- 111 020 spectra from 742 *Apo-Ident* customers from a total of 31 787 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sorbitol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sorbitol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	160	0	118 982
Type C	0	226	1	111 020

The substance/substance group *Sorbitol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	99.5595 % (> 98.2379 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sorbitol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	15.69	—
Xylitol	35.07	—
Isosorbide dinitrate 40%	42.02	—
Pancreas powder	43.28	—
Aciclovir	46.81	—
Potassium citrate	51.21	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sorbitol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21834	21834	0.00	15.29
22293	22293	0.00	15.19
22539	22539	0.00	14.25
22847	21834	1.89	15.63
22849	22849	0.00	14.07
23028	23028	0.00	17.25
23442	23028	2.64	17.24
21485	22293	2.63	15.55

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Soy lecithin (instant form)**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20539-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Soy lecithin (instant form); Lecithinum e sojæ plv.

Special notes

When selecting the *Soy lecithin (instant form)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Soy lecithin (instant form)	4	1	29

Second-stage model

For differentiation of the substance/substance group *Soy lecithin (instant form)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Soy lecithin (instant form)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Soy lecithin (in. ...)	13030504	20985	40	1404399
Caelo	Soy lecithin (in. ...)	13279813	21523	40	20130903
Caelo	Soy lecithin (in. ...)	17118101	23370	40	20170620
Caelo	Soy lecithin (in. ...)	191879	24749	40	20190712*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Soy lecithin (instant form)*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Soy lecithin (instant form)*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Soy lecithin (instant form)	173224	24244	40
Caelo	Soy lecithin (instant form)	17118101	23445	40

- 119062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 55 spectra from 30 *Apo-Ident* customers from 32 batches from the substance/substance group *Soy lecithin (instant form)*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Soy lecithin (instant form)	12139001	3
Caelo	Soy lecithin (instant form)	11371504	1
Caelo	Soy lecithin (instant form)	12139011	3
Caelo	Soy lecithin (instant form)	12139012	1
Caelo	Soy lecithin (instant form)	13030503	1
Caelo	Soy lecithin (instant form)	13030506	1
Caelo	Soy lecithin (instant form)	13279806	1
Caelo	Soy lecithin (instant form)	13279814	1
Caelo	Soy lecithin (instant form)	14281605	1
Caelo	Soy lecithin (instant form)	14281618	4
Caelo	Soy lecithin (instant form)	15262704	4
Caelo	Soy lecithin (instant form)	1526704	1
Caelo	Soy lecithin (instant form)	16223302	2
Caelo	Soy lecithin (instant form)	17081501	1
Caelo	Soy lecithin (instant form)	17118108	1
Caelo	Soy lecithin (instant form)	17118102	1
Caelo	Soy lecithin (instant form)	17322402	1
Caelo	Soy lecithin (instant form)	17322405	3
Caelo	Soy lecithin (instant form)	18282701	1
Caelo	Soy lecithin (instant form)	14281620	1
Caelo	Soy lecithin (instant form)	17118105	1
Caelo	Soy lecithin (instant form)	14281606	2
Caelo	Soy lecithin (instant form)	14196305	1
Caelo	Soy lecithin (instant form)	17322401	2
Caelo	Soy lecithin (instant form)	19009101	2
Caesar & Loretz GmbH	Soy lecithin (instant form)	14281603	1
Caesar & Loretz GmbH, 4...	Soy lecithin (instant form)	12139013	1
Caesar & Loretz GmbH	Soy lecithin (instant form)	13030503	1
Caesar & Loretz GmbH	Soy lecithin (instant form)	13279813	1
INTR/ Sana	Soy lecithin (instant form)	16223302	1
Sanacorp	Soy lecithin (instant form)	14196305	1
Sanacorp	Soy lecithin (instant form)	17322405	1
Caelo	Soy lecithin (instant form)	15262701	4
siehe WE-Prüfprotokoll	Soy lecithin (instant form)	31/14	1
Caelo	Soy lecithin (instant form)		1
Caelo	Soy lecithin (instant form)	17118101	1

- 111 192 spectra from 742 *Apo-Ident* customers from a total of 31 861 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Soy lecithin (instant form)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Soy lecithin (instant form)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	80	0	119 062
Type C	0	53	2	111 192

The substance/substance group *Soy lecithin (instant form)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	96.3636 % (> 90.9091 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Soy lecithin (instant form)* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Menthol	46.04	—
Ascorbyl palmitate	46.39	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Soy lecithin (instant form)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20985	20985	0.00	45.49
21523	20985	12.14	50.43
23370	20985	9.08	49.65
24749	24749	0.00	49.10

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Spironolactone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21032-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Spironolactone; Spironolactonum

Special notes

When selecting the *Spironolactone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Spironolactone	7	9	128

Second-stage model

For differentiation of the substance/substance group *Spironolactone* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Spironolactone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Spironolactone	14378715	22385	40	20150211
Caelo	Spironolactone	160773	22444	60	20160415*
Caelo	Spironolactone	190158	24548	40	20190308*
Euro OTC	Spironolactone	1212034-01	21032	50	1403151
Euro OTC	Spironolactone	1212034-01	21076	42	20130215
Euro OTC	Spironolactone	1602006	22369	45	20160309*
Fagron	Spironolactone	15G22-B10-311159	22386	40	20150728
Fagron	Spironolactone	2294216E20-B06-322016	22942	40	20160531

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 357 spectra of 8 reference samples from the substance/substance group *Spironolactone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 332 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 360 spectra of 9 reference samples from the substance/substance group *Spironolactone*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Spironolactone	16077305	22954	40
Caelo	Spironolactone	171165	23327	40
Caelo	Spironolactone	172432	23660	40
Caelo	Spironolactone	182080	24391	40
Caelo	Spironolactone	191979	24748	40
Euro OTC	Spironolactone	1612002	22909	40
Euro OTC	Spironolactone	1711013	23888	40
Euro OTC	Spironolactone	1809020	24324	40
Euro OTC	Spironolactone	1907001	24782	40

- 118782 spectra from a total of 2411 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 450 spectra from 188 *Apo-Ident* customers from 136 batches from the substance/substance group *Spironolactone*.
- Among them are spectra of independent samples from 128 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Spironolactone	18208004	5
Alliance Healthcare	Spironolactone	12049129	1
Alliance Healthcare	Spironolactone	12049119	1
apomix	Spironolactone	16077320	1
Caelo	Spironolactone	1438721	1
Caelo	Spironolactone	12049103	1
Caelo	Spironolactone	10159914	1
Caelo	Spironolactone	2013U-03249	1
Caelo	Spironolactone	11042602	1
Caelo	Spironolactone	13124303	7
Caelo	Spironolactone	12049123	3
Caelo	Spironolactone	12049130	4
Caelo	Spironolactone	13124309	4
Caelo	Spironolactone	13124304	7
Caelo	Spironolactone	1314309	1
Caelo	Spironolactone	13124315	6
Caelo	Spironolactone	13124317	3
Caelo	Spironolactone	140202901	1
Caelo	Spironolactone	13124321	2
Caelo	Spironolactone	150401601	1
Caelo	Spironolactone	14378709	4
Caelo	Spironolactone	14378703	1
Caelo	Spironolactone	1437807	1
Caelo	Spironolactone	14378717	3

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Supplier	Substance	Batch	Spectra
Caelo	Spironolactone	16077302	13
Caelo	Spironolactone	14378719	1
Caelo	Spironolactone	16077303	15
Caelo	Spironolactone	15G22-B10	1
Caelo	Spironolactone	14378701	2
Caelo	Spironolactone	16077307	1
Caelo	Spironolactone	16077311	11
Caelo	Spironolactone	16H20-B06-322016	1
Caelo	Spironolactone	16077312	15
Caelo	Spironolactone	17116501	1
Caelo	Spironolactone	16077319	4
Caelo	Spironolactone	16077320	9
Caelo	Spironolactone	17116502	7
Caelo	Spironolactone	171165012	1
Caelo	Spironolactone	16077324	1
Caelo	Spironolactone	16077326	11
Caelo	Spironolactone	16077325	7
Caelo	Spironolactone	16077316	1
Caelo	Spironolactone	22121701	1
Caelo	Spironolactone	18004803	11
Caelo	Spironolactone	18004908	5
Caelo	Spironolactone	18004913	4
Caelo	Spironolactone	18004917	14
Caelo	Spironolactone	18004920	9
Caelo	Spironolactone	18208003	4
Caelo	Spironolactone	18208008	6
Caelo	Spironolactone	18208005	1
Caelo	Spironolactone	19015803	3
Caelo	Spironolactone	16077309	7
Caelo	Spironolactone	14378718	9
Caelo	Spironolactone	5013Q-03249	1
Caelo	Spironolactone	18004904	14
Caelo	Spironolactone	14378721	2
Caelo	Spironolactone	18208010	4
Caelo	Spironolactone	16077306	8
Caelo	Spironolactone	12049110	2
Caelo	Spironolactone	13124314	2
Caelo	Spironolactone	1090216	1
Caelo	Spironolactone	16077312/1230817	1
Caelo	Spironolactone	18004915	8
Caelo	Spironolactone	14378710	4
Caelo	Spironolactone	12049105	2
Caelo	Spironolactone	161200201	1
Caelo	Spironolactone	13190309	1
Caelo	Spironolactone	16D15-B06-320903	1
Caelo	Spironolactone	19015804	3
Caelo	Spironolactone	13124320	3
Caelo	Spironolactone	14378702	3
Caelo	Spironolactone	10H24-N10	1
Caelo	Spironolactone	16A14-B05-317123	1
Caelo	Spironolactone	131243315	1
Caelo	Spironolactone	16077305	7
Caelo	Spironolactone	12049118	3
Caesar & Loretz GmbH	Spironolactone	12049129	1
Caesar & Loretz GmbH	Spironolactone	18208003	3
Caesar & Loretz GmbH	Spironolactone	19015804	1
Caesar & Loretz GmbH / ...	Spironolactone	18004915	1
Caesar u Loretz	Spironolactone	12049119	1
Caesar&lorenz,Anzag	Spironolactone	13124309	1
Caesar&lorenz,Phoenix	Spironolactone	11042613	1

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Supplier	Substance	Batch	Spectra
Caesar&lorenz,Phoenix	Spironolactone	11042603	1
Caesar/Lorenz	Spironolactone	13124303	1
Cealo/Gehe	Spironolactone	18004904	2
EuRho	Spironolactone	1101013-01	1
Euro OTC	Spironolactone	3513E-03249	1
Euro OTC	Spironolactone	14378721	1
Euro OTC	Spironolactone	1907001-01	1
Euro OTC	Spironolactone	1809020-01	2
Euro OTC	Spironolactone	1000403502	1
Euro OTC	Spironolactone	1612002-01	5
Euro OTC	Spironolactone	1101013-01	1
Euro OTC	Spironolactone	1004035	1
Euro OTC	Spironolactone	171101301	1
Euro OTC	Spironolactone	161200201	1
Euro OTC	Spironolactone	1602006-01	1
Euro OTC	Spironolactone	180902001	1
Euro OTC	Spironolactone	1504016-01	1
Euro OTC	Spironolactone	16E20-B06-322016	1
Euro OTC	Spironolactone	1402029-01	1
Euro OTC	Spironolactone	1711013-01	7
Fagron	Spironolactone	12/17-N01	1
Fagron	Spironolactone	13G03-N09	1
Fagron	Spironolactone	13G16-B08	1
Fagron	Spironolactone	13G16-B08-288051	1
Fagron	Spironolactone	80616-7	1
Fagron	Spironolactone	16A14-B05-317123	1
Fagron	Spironolactone	16A14-B05	1
Fagron	Spironolactone	16E20-B06-322016	1
Fagron	Spironolactone	16I06B04329443	1
Fagron	Spironolactone	17H16-B05	2
Fagron	Spironolactone	18208003	1
Fagron	Spironolactone	12I17-N01	1
Fagron	Spironolactone	16I06-B04	1
Fagron	Spironolactone	16A14-B05-525187	1
Fagron	Spironolactone	18A24-B03	1
Fagron	Spironolactone	16I06-B04-329443	1
Fagron	Spironolactone	12J15-N04	1
Fagron	Spironolactone	14B20B06294618	1
Fagron	Spironolactone	16E20-B06-325478	2
Fagron	Spironolactone	14J02-B303621	1
Fagron	Spironolactone	14J02-B02-303621	5
Fagron	Spironolactone	10H24-N10	1
Fagron	Spironolactone	16D15-B06-320903	1
Fagron	Spironolactone	14B20-B06-294618	5
Fagron	Spironolactone	14j02-b02-303621	1
Fagron	Spironolactone	2415E-03249	1
Fagron	Spironolactone	17E22-B11-335454	2
Fagron	Spironolactone	17116502	1
Fagron	Spironolactone	10C29-N09	1
gehe	Spironolactone	17E22-B11-335455	1
Gehe	Spironolactone	12049105	1
Gehe	Spironolactone	13D12-N08	1
Gehe	Spironolactone	17H16-B05-341740	1
Gehe	Spironolactone	18208003	1
Gehe	Spironolactone	19015803	1
GEHE	Spironolactone	16077325	1
Caelo	Spironolactone	1110917/16077320	1
Jenne	Spironolactone	14378715	1
Noweda	Spironolactone	1101013-0	1
Noweda	Spironolactone	14378710	1

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Supplier	Substance	Batch	Spectra
Noweda	Spironolactone	1504016-01	1
Noweda	Spironolactone	1602006-01	1
Noweda	Spironolactone	1612002-01	1
Fagron	Spironolactone	12/17-n01	1
Euro OTC	Spironolactone	16020006-01	1
Phoenix	Spironolactone	18A24-B03-354314	1
Phoenix	Spironolactone	18208008	1
Phoenix	Spironolactone	19C29-B06-191465	1
Phönix	Spironolactone	1101013-03	1
Phönix	Spironolactone	17H16-B05-344771	1
Phönix	Spironolactone	1809020-01	2
Fagron	Spironolactone	17H16-B05-344771	3
Sanacorp	Spironolactone	11042612	1
Sanacorp	Spironolactone	12049103	2
Sanacorp	Spironolactone	12049130	1
Sanacorp	Spironolactone	1212034-01	1
Sanacorp	Spironolactone	18004913	1
Sanacorp	Spironolactone	18208004	1
Sanacorp/Phoenix	Spironolactone	13124315	2
Caelo	Spironolactone	11G28-N03	1
Fagron	Spironolactone	13D12-N08	2
Caelo	Spironolactone	11042607	1
Caelo	Spironolactone	12049109	1
WE Phönix 25.11..2016 ...	Spironolactone	16077303	1
Caelo	Spironolactone	14378715	5
Caelo	Spironolactone		1
Caelo	Spironolactone	160773	1
Euro OTC	Spironolactone	1212034-01	6
Fagron	Spironolactone	15G22-B10-311159	2
Fagron	Spironolactone		1
	Spironolactone		1

- 110 797 spectra from 742 *Apo-Ident* customers from a total of 31 758 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Spironolactone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Spironolactone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	357	0	110 332
Type B	0	360	0	118 782
Type C	0	443	7	110 797

The substance/substance group *Spironolactone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3193 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.3333 %)
Type C	100.0000 % (> 99.8899 %)	98.4444 % (> 97.7778 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Spironolactone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Finasteride (form III)	32.25	—
Budesonide, micronized	40.98	—
Estradiol valerate	43.92	—
Estriol	48.46	74.66
Betamethasone valerate	53.91	—
⋮	⋮	⋮
Progesterone, micronized	>50	61.16
Testosterone propionate	>50	72.64
Pregnenolone	>50	131.85
Alfatradiol	>50	140.56
Quinine hydrochloride	>50	296.34
Quinine sulfate	>50	349.77

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Spironolactone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22444	22444	0.00	40.98
24548	24548	0.00	41.05
22386	22444	2.53	42.60
22369	22369	0.00	41.67
22385	22444	3.15	43.23
21076	21032	2.48	45.20

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22942	22369	1.99	42.10
21032	21032	0.00	43.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Starch**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20790-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Starch; Amylum Maydis; Amylum oryzae; Amylum Solani; Amylum tritici; Corn starch; Potato starch; Rice starch; SyrSpend® SF Alka; SyrSpend® SF pH4; Wheat starch

Special notes

When selecting the *Starch* substance/substance group, the following information is displayed to the user:

- Advice for the identification of SyrSpend® SF Alka: Please shake the sample before the measurement to ensure an even particle distribution.

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Corn starch	3	3	23
Potato starch	4	2	8
Rice starch	4	3	51
SyrSpend® SF Alka	4	1	27
SyrSpend® SF pH4	2	2	18
Wheat starch	4	3	17

Second-stage model

For differentiation of the substance/substance group *Starch* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Starch*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Corn starch	13154914	21827	60	20130529
Caelo	Corn starch	161385	22450	60	20160621*
Caelo	Corn starch	182748	24361	40	20181031*
Caelo	Potato starch	12360213	20996	40	1403494
Caelo	Potato starch	14033815	21965	60	20140207
Caelo	Potato starch	161237	22449	60	20160621*
Klenk	Potato starch	0094A170123	23923	40	20170309
Caelo	Rice starch	12068525	20790	40	20120327
Caelo	Rice starch	16144501	22585	40	20160504
Euro OTC	Rice starch	1912005	25080	40	20200109*
Fagron	Rice starch	16B25-B01-327231	23219	40	20160308
Fagron	Rice starch	16B25-B01-327231	23220	40	AR-17-FG-015298-02
Fagron	SyrSpend [®] SF Alka	17D11-B04-332593	23448	40	20170505
Fagron	SyrSpend [®] SF Alka	17D11-B04-332593	23449	40	20170505
Fagron	SyrSpend [®] SF Alka	17F14-B02-335945	23750	20	1804106
Fagron	SyrSpend [®] SF Alka	18B21-B08-347192	24112	40	1809264
Fagron	SyrSpend [®] SF Alka	18C13-B11-350851	24290	40	20180502
Fagron	SyrSpend [®] SF pH4	15A26-B04-311720	22496	40	1608352
Fagron	SyrSpend [®] SF pH4	15A26-B04-311720	22497	40	20150223
Fagron	SyrSpend [®] SF pH4	15A26-B04-305667	22719	40	1701055
Caelo	Wheat starch	14023203	21447	60	AR-16-FG-011433-01
Caelo	Wheat starch	15124707	22246	60	20150527
Klenk	Wheat starch	0104A141114	21973	60	20141210
Klenk	Wheat starch	0104A160512	23510	40	20160628

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1080 spectra of 24 reference samples from the substance/substance group *Starch*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 21 different batches.
- 109 609 spectra from a total of 1945 batches from further 385 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A*

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 740 spectra of 19 reference samples from the substance/substance group *Starch*.
- Among them are spectra of independent samples from 14 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Corn starch	16138505	23217	40
Caelo	Corn starch	172873	23813	40
Caelo	Corn starch	170474	24037	40
Caelo	Potato starch	15062921	23189	40
Caelo	Potato starch	173003	23811	40
Caelo	Rice starch	162180	22642	40
Caelo	Rice starch	190169	24551	40
Caelo	Rice starch	190168	24553	40
Fagron	SyrSpend [®] SF Alka	15H11-B04-311722	22494	40
Fagron	SyrSpend [®] SF pH4	15H13-B03-314611	23450	40
Fagron	SyrSpend [®] SF pH4	16J10-B03-330757	23749	40
Caelo	Wheat starch	15421507	23509	40
Caelo	Wheat starch	181200	24014	40
Caelo	Wheat starch	192516	24885	40
Fagron	SyrSpend [®] SF Alka	15H11-B04-311722	22495	40
Fagron	SyrSpend [®] SF Alka	15H11-B04-311722	22718	40
Fagron	SyrSpend [®] SF Alka	17F14-B02-335945	23750 [†]	20
Fagron	SyrSpend [®] SF Alka	15H11-B04-311722	23768	40
Fagron	SyrSpend [®] SF pH4	15H13-B03-314611	23451	40

- 118402 spectra from a total of 2405 batches from further 794 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 372 spectra from 172 *Apo-Ident* customers from 146 batches from the substance/substance group *Starch*.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- Among them are spectra of independent samples from 131 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Corn starch	15310914	5
Caelo	Corn starch	11179307	2
Caelo	Corn starch	12238705	1
Caelo	Corn starch	12238715	2
Caelo	Corn starch	15310909	2
Caelo	Corn starch	15310904	1
Caelo	Corn starch	15310908	1
Caelo	Corn starch	16138505	4
Caelo	Corn starch	16138507	2
Caelo	Corn starch	14111701	1
Caelo	Corn starch	17047404	6
Caelo	Corn starch	64A170123	1
Caelo	Corn starch	18274802	1
Caelo	Corn starch	15310902	2
Caelo	Corn starch	18274804	1
Caelo/Sanacorp	Corn starch	17287302	1
Fagron	Corn starch	17287302	1
Fagron	Corn starch	15310902	1
Klenk	Corn starch	4263535	1
Klenk	Corn starch	64A170123	7
Caelo	Corn starch	10061146	1
Caelo	Corn starch	15310903	3
Caelo	Corn starch	17287302	2
Bombastus	Potato starch	12214303	2
Caelo	Potato starch	11301012	2
Caelo	Potato starch	15062912	2
Caelo	Potato starch	17327201	3
Caelo	Potato starch	17037404	1
Klenk	Potato starch	94A170123	3
Klenk	Potato starch	94A110512	1
Klenk	Potato starch	94a170123	1
Caelo	Rice starch	16101401	1
Caelo	Rice starch	11132406	1
Caelo	Rice starch	12238714	1
Caelo	Rice starch	13154904	3
Caelo	Rice starch	10061134	2
Caelo	Rice starch	200613K3	1
Caelo	Rice starch	64A130304	6
Caelo	Rice starch	14025710	1
Caelo	Rice starch	13005908	1
Caelo	Rice starch	13305108	1
Caelo	Rice starch	14301214	1
Caelo	Rice starch	14025733	1
Caelo	Rice starch	16144506	1
Caelo	Rice starch	17173501	2
Caelo	Rice starch	16218009	1
Caelo	Rice starch	17327503	2
Caelo	Rice starch	17327502	1
Caelo	Rice starch	14011612	3
Caelo	Rice starch	16218002	1
Caelo	Rice starch	12214303	1
Caelo	Rice starch	104A120621	1
Caelo	Rice starch	12166007	3
Caelo	Rice starch	11186026	1
Caelo	Rice starch	14011621	1
Caelo	Rice starch	104A141114	3
Caelo	Rice starch	13305103	3

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Supplier	Substance	Batch	Spectra
Caelo	Rice starch	14011630	2
Caelo	Rice starch	9352108	1
Caelo	Rice starch	2212M-01115	1
Caelo	Rice starch	15119011	6
Caelo	Rice starch	13005905	2
Caelo	Rice starch	14025734	1
Caelo	Rice starch	12238719	1
Caelo	Rice starch	15118607	1
Cealo	Rice starch	13305103	1
Fagron	Rice starch	12L19-N06	1
Fagron	Rice starch	14F18-B04-301616	1
Caelo	Rice starch	16218013	1
Gutenberg-Apotheke	Rice starch	12360216	1
Klenk	Rice starch	84A141114	3
Klenk	Rice starch	64A130304	16
Klenk	Rice starch	104A130304	8
Klenk	Rice starch	104A141114	9
Klenk	Rice starch	64A080218	5
Klenk	Rice starch	94A130304	5
Klenk	Rice starch	64a130304	1
Klenk	Rice starch	84A130304	1
Klenk	Rice starch	104A120621	5
Klenk	Rice starch	94A100122	1
Koisser	Rice starch	WE07032013	1
Nachprüfung	Rice starch	3709E01116	1
Noweda	Rice starch	14023203	1
Noweda	Rice starch	14011621	1
phönix	Rice starch	84a141114	1
sanacorp	Rice starch	94A130304	1
Sanacorp	Rice starch	84A141114	1
Caelo	Rice starch	10177515	1
Caelo	Rice starch	10177507	1
VDL;03.03.15;3,04EUR	Rice starch	14011627	1
VDL;3,03EUR;11.06.15	Rice starch	14011630	1
Fagron	SyrSpend [®] SF Alka	15K03-B01-525173	1
Caelo	SyrSpend [®] SF Alka	18871B06	1
Caelo	SyrSpend [®] SF Alka	18C13-B11-350851	1
Caelo	SyrSpend [®] SF Alka	353473	1
Caelo	SyrSpend [®] SF Alka	18J25-B15-357803	2
Caelo	SyrSpend [®] SF Alka	720026-000	1
Fagron	SyrSpend [®] SF Alka	17D11-B04	2
Fagron	SyrSpend [®] SF Alka	17D11-bo4-332593	1
Fagron	SyrSpend [®] SF Alka	18821-b08-347192	1
Fagron	SyrSpend [®] SF Alka	18L25-B15-357803	1
Fagron	SyrSpend [®] SF Alka	18J25-B15	1
Fagron	SyrSpend [®] SF Alka	18H01-B12353473	1
Fagron	SyrSpend [®] SF Alka	18B21-B08	1
Fagron	SyrSpend [®] SF Alka	17D11-804-332593	1
Fagron	SyrSpend [®] SF Alka	19F06-B02-363789	2
Fagron	SyrSpend [®] SF Alka	18A26-Bo5-346410	1
Fagron	SyrSpend [®] SF Alka	18A26-B05-346410	1
Fagron	SyrSpend [®] SF Alka	18C13_B11_350851	1
Fagron	SyrSpend [®] SF Alka	18125-B15-357803	1
Fagron	SyrSpend [®] SF Alka	14J22-B40-311723	1
Fagron	SyrSpend [®] SF Alka	18821-B08-347192	2
Fagron	SyrSpend [®] SF Alka	18J25-B15-357803	12
Fagron	SyrSpend [®] SF Alka	17F14-B05-525556	1
Fagron	SyrSpend [®] SF Alka	18L21-B11-359901	3
Fagron	SyrSpend [®] SF Alka	18L21-B11	1
Fagron	SyrSpend [®] SF Alka	19D29-B07-362182	4

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Supplier	Substance	Batch	Spectra
Fagron	SyrSpend [®] SF Alka	16B03-B07-525234	1
Fagron	SyrSpend [®] SF Alka	18H01-B12-353473	11
Gehe	SyrSpend [®] SF Alka	18A26-B05-346410	1
Gehe	SyrSpend [®] SF Alka	18H01-B12-353473	9
Phoenix	SyrSpend [®] SF Alka	18L21-B11-359901	6
Phoenix	SyrSpend [®] SF Alka	19D29-B07-362182	4
Phoenix	SyrSpend [®] SF Alka	19D29-B11-363786	3
Phönix	SyrSpend [®] SF Alka	18B13-B11-350851	1
Phönix/Fagon	SyrSpend [®] SF Alka	17D11-B04-332593	1
Fagron	SyrSpend [®] SF pH4	16J10-B03	1
Caelo	SyrSpend [®] SF pH4	16J10-B03-330757	1
Caelo	SyrSpend [®] SF pH4	18A22-B05-346147	1
Euro OTC	SyrSpend [®] SF pH4	18A22-B05-347899	1
Fagron	SyrSpend [®] SF pH4	16J10-B03-330757	5
Fagron	SyrSpend [®] SF pH4	16/10-B03	1
Fagron	SyrSpend [®] SF pH4	18A22-B05-346147	3
Fagron	SyrSpend [®] SF pH4	18A22-B05-347899	2
Fagron	SyrSpend [®] SF pH4	19A14-B07_362431	1
Fagron	SyrSpend [®] SF pH4	18H30-B02-355226	1
Fagron	SyrSpend [®] SF pH4	18A22-B04_346147	1
Fagron	SyrSpend [®] SF pH4	18H30-B02	1
Fagron	SyrSpend [®] SF pH4	18J16-B01_357703	1
Fagron	SyrSpend [®] SF pH4	18H30-B02_355226	2
Fagron	SyrSpend [®] SF pH4	19J10-F08-366993	1
Fagron	SyrSpend [®] SF pH4	16j10-b03-330757	1
Fagron	SyrSpend [®] SF pH4	16J10B03	1
Gehe	SyrSpend [®] SF pH4	18J16-B01-357703	3
Fagron	SyrSpend [®] SF pH4	18A22-B05	2
Phoenix	SyrSpend [®] SF pH4	16J10-B03-330757	3
Phoenix	SyrSpend [®] SF pH4	18J25-B15-357803	1
Phönix	SyrSpend [®] SF pH4	18H30-B02-355226	8
Anzag 05.03.13 ek: 9,65EUR	Wheat starch	104A120621	2
Caelo	Wheat starch	1114611	1
Caelo	Wheat starch	1512477	1
Caelo	Wheat starch	16162905	3
Caelo	Wheat starch	17183201	1
Caelo	Wheat starch	15421507	2
Caelo	Wheat starch	11350907	1
Caelo	Wheat starch	11350911	2
Caelo	Wheat starch	15124710	1
Caesar & Loretz GmbH	Wheat starch	16162908	1
Euro OTC	Wheat starch	104A171122	1
Fiebig 16.01.13 ek: 4,18EUR	Wheat starch	11350911	1
Fresenius	Wheat starch	13305103	1
Klenk	Wheat starch	104A101116	1
Kehr	Wheat starch	104A160512	1
Klenk	Wheat starch	104a160512	1
Klenk	Wheat starch	104a171122	1
Klenk	Wheat starch	104a141114	1
Klenk	Wheat starch	10A160512	1
Klenk	Wheat starch	104A160512	8
Klenk	Wheat starch	104A171122	5
Klosterring	Wheat starch	15421507	1
Caelo	Wheat starch	18120004	1
PHÖNIX	Wheat starch	16162905	1
Caelo	Corn starch	13154914	2
Caelo	Potato starch	14033815	1
Caelo	Rice starch	14023203	3
Fagron	SyrSpend [®] SF Alka	17D11-B04-332593	3
Fagron	SyrSpend [®] SF Alka	17F14-B02-335945	1

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Supplier	Substance	Batch	Spectra
Fagron	SyrSpend [®] SF Alka	18C13-B11-350851	3
Caelo	Wheat starch	15124707	1

- 110 875 spectra from 742 *Apo-Ident* customers from a total of 31 746 batches from a further 701 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Starch* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Starch* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	1080	0	109 609
Type B	0	740	0	118 395
Type C	0	369	3	110 871

The substance/substance group *Starch* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.4444 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.1892 %)
Type C	100.0000 % (> 99.8900 %)	99.1935 % (> 98.3871 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Starch* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Acacia, dried dispersion	16.00	—
Carmellose sodium (400 / 450 / 500 / 6...	25.04	—
Hyaluronic acid sodium salt	27.14	—
Heparin sodium	51.71	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Starch* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23448	24112	6.32	17.59
23449	24112	7.30	17.16
23750	23750	0.00	19.21
24112	24112	0.00	22.03
24290	24112	3.20	21.38
21973	22450	3.06	29.72
21827	22450	4.05	28.46
22246	24361	7.19	28.42
24361	24361	0.00	29.32
23510	22450	5.86	29.57
20996	20996	0.00	43.32
21965	22449	3.64	45.42
22449	22449	0.00	38.73
23923	22449	5.70	42.03
22496	22496	0.00	14.93
22497	22496	1.27	14.96
22719	22719	0.00	16.00
20790	22450	4.83	25.88
22585	24361	2.75	27.29
23219	23220	3.71	27.07
23220	23220	0.00	28.15
25080	25080	0.00	25.11
22450	22450	0.00	26.68
21447	21447	0.00	23.37

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Stearic acid 50**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20869-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Stearic acid 50; Acidum stearicum

Special notes

When selecting the *Stearic acid 50* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Stearic acid 50	5	2	20

Second-stage model

For differentiation of the substance/substance group *Stearic acid 50* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Stearic acid 50*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Stearic acid 50	12241910	20869	40	AR-15-FG-007284-01
Caelo	Stearic acid 50	14359310	21793	60	20150126
Caelo	Stearic acid 50	14359310	21928	60	AR-16-FG-004044-01
Caelo	Stearic acid 50	14359314	22274	60	20150126
Caelo	Stearic acid 50	170810	23294	40	20170426*
Caelo	Stearic acid 50	170810	23667	40	20170426*
Caelo	Stearic acid 50	192910	25066	40	20191128*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 7 reference samples from the substance/substance group *Stearic acid 50*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 349 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Stearic acid 50*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Stearic acid 50	163469	23032	40
Caelo	Stearic acid 50	180809	24036	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 37 spectra from 21 *Apo-Ident* customers from 22 batches from the substance/substance group *Stearic acid 50*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Stearic acid 50	11103706	1
Caelo	Stearic acid 50	12241914	1
Caelo	Stearic acid 50	16096311	1
Caelo	Stearic acid 50	1609611	1
Caelo	Stearic acid 50	1617081006	1
Caelo	Stearic acid 50	17081006	3
Caelo	Stearic acid 50	18080901	2
Caelo	Stearic acid 50	18080913	2
Caelo	Stearic acid 50	18238006	1
Caelo	Stearic acid 50	18238004	1
Caelo	Stearic acid 50	16096301	1
Caelo	Stearic acid 50	12241915	2
Caelo	Stearic acid 50	18238010	1
Caelo	Stearic acid 50	12241930	3
Caelo	Stearic acid 50	17081003	1
Caelo	Stearic acid 50	11308505	1
Caelo	Stearic acid 50	11308514	1
Caelo	Stearic acid 50	12241911	2
Caesar & Loretz	Stearic acid 50	14359310	1
Caesar & Loretz GmbH/No...	Stearic acid 50	18238006	1
Caesar&Loretz GmbH/Anzag	Stearic acid 50	11308505	1
GEHE	Stearic acid 50	18238006	1
Kehr	Stearic acid 50	16346902	1
Phoenix	Stearic acid 50	12241915	1
Phönix	Stearic acid 50	1224915	1
Caelo	Stearic acid 50	14359314	4

- 111 210 spectra from 742 *Apo-Ident* customers from a total of 31 869 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are docu-

mented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Stearic acid 50* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Stearic acid 50* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	80	0	119 062
Type C	0	37	0	111 210

The substance/substance group *Stearic acid 50* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 83.7838 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Stearic acid 50* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium stearate	43.64	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Stearic acid 50* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20869	20869	0.00	63.21
21793	25066	3.40	61.23
21928	21928	0.00	66.26
22274	25066	3.67	60.12
23294	23294	0.00	59.49
23667	23667	0.00	59.24
25066	25066	0.00	60.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sucrose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20372-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sucrose; Saccharum

Special notes

When selecting the *Sucrose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sucrose	10	4	331

Second-stage model

For differentiation of the substance/substance group *Sucrose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sucrose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sucrose	13352909	21484	40	1410501
Caelo	Sucrose	14340003	21736	60	20141114
Caelo	Sucrose	161999	22615	40	20160714*
Caelo	Sucrose	162060	22643	40	20160808*
Caelo	Sucrose	163286	23057	40	20161219*
Caelo	Sucrose	163081	23058	40	20161115*
Caelo	Sucrose	171066	23297	40	20170511*
Caelo	Sucrose	172133	23666	40	20170817*
Caelo	Sucrose	173247	23833	40	20180117*
Caelo	Sucrose	181582	24217	40	20180605*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 420 spectra of 10 reference samples from the substance/substance group *Sucrose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 269 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Sucrose*.
- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sucrose	12146801	20909	40
Caelo	Sucrose	181546	24237	40
Caelo	Sucrose	182574	24353	40
Caelo	Sucrose	182818	24359	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 687 spectra from 198 *Apo-Ident* customers from 334 batches from the substance/substance group *Sucrose*.
- Among them are spectra of independent samples from 330 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Sucrose	15182805	1
AHD	Sucrose	18154602	1
Audor Pharma	Sucrose	16206102	1
Bombastus	Sucrose	15156008	1
Cael	Sucrose	15182804	3
Caelo	Sucrose	12241804	2
Caelo	Sucrose	12241808	5
Caelo	Sucrose	13031405	3
Caelo	Sucrose	12107805	1
Caelo	Sucrose	28081308	1
Caelo	Sucrose	13031406	2
Caelo	Sucrose	130031417	1
Caelo	Sucrose	20011401	1
Caelo	Sucrose	13352901	2
Caelo	Sucrose	13352908	1
Caelo	Sucrose	13352920	5
Caelo	Sucrose	13352916	3
Caelo	Sucrose	15156008	1
Caelo	Sucrose	14197302	3
Caelo	Sucrose	14197313	1
Caelo	Sucrose	20031515	1
Caelo	Sucrose	14340004	4
Caelo	Sucrose	28041504	1
Caelo	Sucrose	1430009	1
Caelo	Sucrose	24061502	1
Caelo	Sucrose	29081502	1
Caelo	Sucrose	15028802	7
Caelo	Sucrose	154460	1
Caelo	Sucrose	16049907	13
Caelo	Sucrose	160499	1
Caelo	Sucrose	16049902	3
Caelo	Sucrose	162061	1
Caelo	Sucrose	16051305	2
Caelo	Sucrose	16206102	12

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Supplier	Substance	Batch	Spectra
Caelo	Sucrose	16328607	12
Caelo	Sucrose	1649902	1
Caelo	Sucrose	13111706	1
Caelo	Sucrose	17042103	2
Caelo	Sucrose	17106604	10
Caelo	Sucrose	17106601	1
Caelo	Sucrose	18024405	13
Caelo	Sucrose	18024407	2
Caelo	Sucrose	17247203	1
Caelo	Sucrose	18154603	14
Caelo	Sucrose	27111802	1
Caelo	Sucrose	18257401	4
Caelo	Sucrose	18281803	1
Caelo	Sucrose	19132301	1
Caelo	Sucrose	14340009	4
Caelo	Sucrose	18154602	3
Caelo	Sucrose	14197301	4
Caelo	Sucrose	1352920	1
Caelo	Sucrose	16206103	5
Caelo	Sucrose	13031409	1
Caelo	Sucrose	15446002	9
Caelo	Sucrose	15028801	13
Caelo	Sucrose	13031417	2
Caelo	Sucrose	14340008	1
Caelo	Sucrose	18329703	1
Caelo	Sucrose	18281804	6
Caelo	Sucrose	16328606	3
Caelo	Sucrose	15182805	3
Caelo	Sucrose	16051304	1
Caelo	Sucrose	12107806	2
Caelo	Sucrose	18329702	5
Caelo	Sucrose	17288702	1
Caelo	Sucrose	15446007	1
Caelo	Sucrose	16328603	8
Caelo	Sucrose	13063907	1
Caelo	Sucrose	12241817	2
Caelo	Sucrose	13031414	1
Caelo	Sucrose	11246313	2
Caelo	Sucrose	13031410	2
Caelo	Sucrose	13352902	13
Caelo	Sucrose	81172478	2
Caelo	Sucrose	13352905	1
Caelo	Sucrose	13352911	1
Caelo	Sucrose	14340005	1
Caelo	Sucrose	15446003	6
Caelo	Sucrose	14340006	1
Caelo	Sucrose	16051301	1
Caelo	Sucrose	16328605	17
Caelo	Sucrose	17106603	41
Caelo	Sucrose	15182804	20
Caelo	Sucrose	17354506	10
Caelo	Sucrose	1802445	1
Caelo	Sucrose	19062701	4
Caelo	Sucrose	18281810	1
Caelo	Sucrose	12280309	1
Caelo	Sucrose	16166003	1
Caelo	Sucrose	17021620306	1
Caelo	Sucrose	8024405	1
Caelo	Sucrose	18257402	18
Caeolo/Gehe	Sucrose	15446002	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Sucrose	18257402	2
Caesar & Loretz GmbH	Sucrose	18154601	1
Caesar & Loretz GmbH	Sucrose	19062701	1
Caesar & Loretz GmbH	Sucrose	19062706	1
Caesar & Loretz GmbH	Sucrose	190627002	1
Caesar & Loretz GmbH / ...	Sucrose	16049907	1
Caesar & Loretz GmbH/G	Sucrose	18257402	1
DHU	Sucrose	9010710	1
DHU	Sucrose	9020510	1
DHU	Sucrose	9010709	1
DHU	Sucrose	7020407	1
DHU	Sucrose	9020110	1
DHU	Sucrose	9050610	1
Diamant	Sucrose	L24223	1
Euro OTC	Sucrose	12345	2
Euro OTC	Sucrose	16328605	1
Euro OTC	Sucrose	18024405	2
Fagron	Sucrose	5112I-02207	1
Fagron	Sucrose	12-E03-M01	1
Fagron	Sucrose	13G03-N16	1
Fagron	Sucrose	1011208731	2
Fagron	Sucrose	2102308731	1
Fagron	Sucrose	18082014D	1
Fagron	Sucrose	11/20-N05	1
Fagron	Sucrose	5071201	1
Fagron	Sucrose	12G26-N01	2
Fagron	Sucrose	13G04-N01	1
Fagron	Sucrose	15446002	1
Fagron	Sucrose	16206102	1
Fagron	Sucrose	18257402	1
Fagron	Sucrose	11I16-N01	1
Fagron	Sucrose	13A07-N03	1
Fagron	Sucrose	12E29-N04	1
Fagron	Sucrose	13D29-N08	1
Fagron	Sucrose	13I30-N05	1
Fagron	Sucrose	11/16-N01	1
Fagron	Sucrose	11L09-N16	2
Fagron	Sucrose	11E19-N04	1
Fagron	Sucrose	11/16-N01	1
Gehe	Sucrose	16328607	1
Gehe	Sucrose	17106603	1
Gehe	Sucrose	18329702	1
GEHE	Sucrose	16328607	1
Hanns G.Werner GmbH	Sucrose	8731158	1
Haushalt	Sucrose	123456	1
Jenne	Sucrose	15182804	1
Jenne	Sucrose	18257402	1
Caelo	Sucrose	190627002	1
Kaufland	Sucrose	L24475	1
Kaufland	Sucrose	L24494	2
Kehr	Sucrose	16328606	1
L12	Sucrose	18154603	1
Noweda	Sucrose	13352920	2
Noweda	Sucrose	16328607	1
Noweda	Sucrose	18154603	1
Caelo	Sucrose	11246306	1
Penny	Sucrose	L12513800	3
Penny Markt	Sucrose	L120325600	2
Penny Markt	Sucrose	L120404100	3
Penny Markt	Sucrose	201L113530100	3

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Supplier	Substance	Batch	Spectra
Penny Markt	Sucrose	L120612100	3
Penny Markt	Sucrose	L120628000	3
Pfeifer/Langen	Sucrose	L03144N	1
Pharmachem	Sucrose	7878	1
pharm-a-speres	Sucrose	8731003	1
pharm-a-spheres/sana 23. ...	Sucrose	8731306	1
Phoenix	Sucrose	18257402	1
phönix	Sucrose	16351701	1
Phönix	Sucrose	15446002	1
PHÖNIX	Sucrose	17106603	1
Sanacorp	Sucrose	14340005	1
Sanacorp	Sucrose	AKD5	1
Sanacorp/Caela	Sucrose	17106603	1
Soldan	Sucrose	232027	1
Soldan	Sucrose	243983	1
Spagyra	Sucrose	12082320717	1
Spagyra	Sucrose	12103020975	1
Spagyra	Sucrose	13040921431	1
Spagyra	Sucrose	13040921430	1
Spagyra	Sucrose	13012920302	1
Spagyra	Sucrose	13040921424	1
Spagyra	Sucrose	13020620240	1
Spagyra	Sucrose	13030621373	1
Spagyra	Sucrose	13040921427	1
Spagyra	Sucrose	13041920152	2
Spagyra	Sucrose	13041920154	1
Spagyra	Sucrose	13051520939	1
Spagyra	Sucrose	13051520941	1
Spagyra	Sucrose	13061020526	1
Spagyra	Sucrose	13061020525	1
Spagyra	Sucrose	13061020529	1
Spagyra	Sucrose	13061020524	1
Spagyra	Sucrose	13061020528	1
Spagyra	Sucrose	13061220385	2
Spagyra	Sucrose	13050621773	2
Spagyra	Sucrose	13070420937	2
Spagyra	Sucrose	13070420936	2
Spagyra	Sucrose	13070420938	1
Spagyra	Sucrose	13072620834	1
Spagyra	Sucrose	16032920732	1
Spagyra	Sucrose	16042522126	1
Spagyra	Sucrose	16053020827	1
Spagyra	Sucrose	16050220821	1
Spagyra	Sucrose	16051820801	1
Spagyra	Sucrose	5030921075	1
Spagyra	Sucrose	16050421023	1
Spagyra	Sucrose	16070421669	1
Spagyra	Sucrose	5030920997	1
Spagyra	Sucrose	5030920996	1
Spagyra	Sucrose	5030920998	1
Spagyra	Sucrose	5030921004	1
Spagyra	Sucrose	5030920873	1
Spagyra	Sucrose	5030920989	1
Spagyra	Sucrose	5030920995	1
Spagyra	Sucrose	5030921221	1
Spagyra	Sucrose	5030921002	1
Spagyra	Sucrose	5030921096	1
Spagyra	Sucrose	5030921012	1
Spagyra	Sucrose	5030921015	1
Spagyra	Sucrose	5030921016	1

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Supplier	Substance	Batch	Spectra
Spagyra	Sucrose	5030920923	1
Spagyra	Sucrose	5030921020	1
Spagyra	Sucrose	5030920922	1
Spagyra	Sucrose	5030920883	1
Spagyra	Sucrose	5030920881	1
Spagyra	Sucrose	5030921014	1
Spagyra	Sucrose	10073020385	1
Spagyra	Sucrose	7062220875	1
Spagyra	Sucrose	5030921010	1
Spagyra	Sucrose	5030921082	1
Spagyra	Sucrose	5030921019	1
Spagyra	Sucrose	5030921024	1
Spagyra	Sucrose	5030921026	1
Spagyra	Sucrose	5030920999	1
Spagyra	Sucrose	5030921028	1
Spagyra	Sucrose	5030921031	1
Spagyra	Sucrose	15082720411	1
Spagyra	Sucrose	5030921030	1
Spagyra	Sucrose	5030921006	1
Spagyra	Sucrose	5030921032	1
Spagyra	Sucrose	5030921041	1
Spagyra	Sucrose	5030921040	1
Spagyra	Sucrose	5030921036	1
Spagyra	Sucrose	5030921042	1
Spagyra	Sucrose	5030921038	1
Spagyra	Sucrose	5030921064	1
Spagyra	Sucrose	5030921039	1
Spagyra	Sucrose	5030921043	1
Spagyra	Sucrose	5030920885	1
Spagyra	Sucrose	5030921037	1
Spagyra	Sucrose	5030921054	1
Spagyra	Sucrose	5030921053	1
Spagyra	Sucrose	5030921101	1
Spagyra	Sucrose	5030921122	1
Spagyra	Sucrose	5030921100	1
Spagyra	Sucrose	5030921056	1
Spagyra	Sucrose	5030921060	1
Spagyra	Sucrose	5030921152	1
Spagyra	Sucrose	5030921065	1
Spagyra	Sucrose	5030920924	1
Spagyra	Sucrose	5030921067	1
Spagyra	Sucrose	5030921078	1
Spagyra	Sucrose	5030921081	1
Spagyra	Sucrose	5030921072	1
Spagyra	Sucrose	5030920908	1
Spagyra	Sucrose	5030920893	1
Spagyra	Sucrose	5030921080	1
Spagyra	Sucrose	5030921094	1
Spagyra	Sucrose	5030920895	1
Spagyra	Sucrose	5030921090	1
Spagyra	Sucrose	10032921256	1
Spagyra	Sucrose	15032620414	1
Spagyra	Sucrose	16083120745	1
Spagyra	Sucrose	1905	1
Spagyra	Sucrose	1918	1
Spagyra	Sucrose	2007	1
Spagyra	Sucrose	1691	1
Spagyra	Sucrose	1911	1
Spagyra	Sucrose	16102120418	1
Spagyra	Sucrose	16110320884	1

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Supplier	Substance	Batch	Spectra
Spagyra	Sucrose	17072120538	1
Spagyra	Sucrose	2923	1
Spagyra	Sucrose	17082320366	1
Spagyra	Sucrose	17072120536	1
Spagyra	Sucrose	17072120537	1
Spagyra	Sucrose	17070420968	1
Spagyra	Sucrose	17080920574	1
Spagyra	Sucrose	17090620617	1
Spagyra	Sucrose	3750	1
Spagyra	Sucrose	18081720533	1
Spagyra Österreich	Sucrose	15112321097	1
Spagyra/Österreich	Sucrose	16122820921	1
Spagyra/Österreich	Sucrose	17021620307	1
Spagyra/Österreich	Sucrose	17020820816	1
Spagyra/Österreich	Sucrose	17021620309	1
Spagyra/Österreich	Sucrose	17020820810	1
Spagyra/Österreich	Sucrose	17032820797	1
Spagyra/Österreich	Sucrose	17032321132	1
Spagyra/Österreich	Sucrose	17032120927	1
Spagyra/Österreich	Sucrose	17022022188	1
Spagyra/Österreich	Sucrose	17041821026	1
Spagyra/Österreich	Sucrose	17041821027	1
Spagyra/Österreich	Sucrose	2307	2
Spagyra/Österreich	Sucrose	17070320627	1
Spagyra/Österreich	Sucrose	2382	1
Spagyra/Österreich	Sucrose	17092620773	1
Spagyra/Österreich	Sucrose	17091520139	1
Spagyra/Österreich	Sucrose	H17-0047	1
Spagyra/Österreich	Sucrose	2963	1
Spagyra/Österreich	Sucrose	2516	1
Spagyra/Österreich	Sucrose	17121420710	1
Spagyra/Österreich	Sucrose	3303	1
Spagyra/Österreich	Sucrose	1721420709	1
Spagyra/Österreich	Sucrose	18021921250	1
Spagyra/Österreich	Sucrose	3183	1
Spagyra/Österreich	Sucrose	18032320388	1
Spagyra/Österreich	Sucrose	H18-0021	1
Spagyra/Österreich	Sucrose	3082	1
Spagyra/Österreich	Sucrose	18032320386	1
Spagyra/Österreich	Sucrose	18032320385	1
Spagyra/Österreich	Sucrose	18032320387	1
Spagyra/Österreich	Sucrose	18041180714	1
Spagyra/Österreich	Sucrose	18041120712	1
Spagyra/Österreich	Sucrose	18042720542	1
Spagyra/Österreich	Sucrose	3071	1
Spagyra/Österreich	Sucrose	18042720555	2
Spagyra/Österreich	Sucrose	18051421069	1
Spagyra/Österreich	Sucrose	18051421071	1
Spagyra/Österreich	Sucrose	18072420037	1
Spagyra/Österreich	Sucrose	13021920149	1
Spagyra/Österreich	Sucrose	14070721041	1
Spagyra/Österreich	Sucrose	12112721050	1
Spagyra/Österreich	Sucrose	14012420377	1
Spagyra/Österreich	Sucrose	14071421137	2
Spagyra/Österreich	Sucrose	13050621774	1
Spagyra/Österreich	Sucrose	14060353342	1
Spagyra/Österreich	Sucrose	14010721509	1
Spagyra/Österreich	Sucrose	13091920456	1

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Supplier	Substance	Batch	Spectra
Spagyra/Österreich	Sucrose	14050621091	1
Spagyra/Österreich	Sucrose	1624	1
Spagyra/Österreich	Sucrose	13111121193	1
Spagyra/Österreich	Sucrose	13102520353	1
Spagyra/Österreich	Sucrose	14060353343	1
Spagyra/Österreich	Sucrose	14041421810	1
Spagyra/Österreich	Sucrose	5030920991	1
Spagyra/Österreich	Sucrose	5030921018	1
Spagyra/Österreich	Sucrose	5030921008	1
Spagyra/Österreich	Sucrose	5030920993	1
Spagyra/Österreich	Sucrose	10070521044	1
Spagyra/Österreich	Sucrose	18090520789	1
Spagyra/Österreich	Sucrose	18090520788	1
Spagyra/Österreich	Sucrose	18090520787	3
Spagyra/Österreich	Sucrose	18091020640	1
Spagyra/Österreich	Sucrose	H18-0210	1
Spagyra/Österreich	Sucrose	1809272503	1
Spagyra/Österreich	Sucrose	18092720503	1
St. Erhard Apotheke	Sucrose	18090520795	1
St. Erhard Apotheke	Sucrose	18090520794	1
St. Erhard Apotheke	Sucrose	18090520790	1
St. Erhard Apotheke	Sucrose	18090520791	1
St. Erhard Apotheke	Sucrose	18090520793	1
St. Erhard Apotheke	Sucrose	1809052072	1
St. Erhard Apotheke	Sucrose	18090520792	1
Staufenpharma	Sucrose	3314E-01586	1
Staufen-Pharma	Sucrose	161112	2
Caelo	Sucrose	12241801	1
Caelo	Sucrose	12241803	2
Werner	Sucrose	1901208731	2
Caelo	Sucrose	13352909	4
Caelo	Sucrose	14340003	3
Caelo	Sucrose		1
	Sucrose	13352908	1
Soldan	Sucrose		1

- 110 560 spectra from 742 *Apo-Ident* customers from a total of 31 563 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sucrose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sucrose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	420	0	110 269
Type B	0	120	40	118 982
Type C	0	652	35	110 560

The substance/substance group *Sucrose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5714 %)
Type B	100.0000 % (> 99.9893 %)	75.0000 % (> 73.1250 %)
Type C	100.0000 % (> 99.8899 %)	94.9054 % (> 94.4687 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sucrose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Wheat starch	33.13	—
SyrSpend® SF Alka	36.29	—
Potato starch	38.39	—
Rice starch	39.13	—
Aciclovir	46.37	—
Fructose	46.88	—
Acacia, dried dispersion	46.92	—
Corn starch	49.35	—
Hyaluronic acid sodium salt	54.41	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sucrose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21484	21484	0.00	31.07
21736	21484	0.81	32.19
22615	22615	0.00	32.26
22643	22643	0.00	34.82
23057	23057	0.00	30.38

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23058	23058	0.00	32.96
23297	23297	0.00	31.89
23666	23666	0.00	33.82
23833	23833	0.00	31.42
24217	24217	0.00	35.16

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sulfacetamide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20695-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sulfacetamide; Sulfacetamidum

Special notes

When selecting the *Sulfacetamide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sulfacetamide	4	3	24

Second-stage model

For differentiation of the substance/substance group *Sulfacetamide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sulfacetamide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sulfacetamide	11085910	20695	40	1402651
Caelo	Sulfacetamide	15445901	23251	40	20160126
Caelo	Sulfacetamide	15445901	23456	40	20160126
Euro OTC	Sulfacetamide	1312012-01	21633	60	20140117
Euro OTC	Sulfacetamide	1509018	21902	60	20150929*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Sulfacetamide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Sulfacetamide*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Sulfacetamide	1702006	23157	40
Euro OTC	Sulfacetamide	1808035	24193	40
Euro OTC	Sulfacetamide	1907026	24804	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 71 spectra from 32 *Apo-Ident* customers from 27 batches from the substance/substance group *Sulfacetamide*.
- Among them are spectra of independent samples from 24 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHC 12.08.13 EK9,31	Sulfacetamide	11085912	1
Caelo	Sulfacetamide	15445905	1
Euro OTC	Sulfacetamide	1112032-01	3
Caelo	Sulfacetamide	11085914	2
Caelo	Sulfacetamide	11085912	4
Caelo	Sulfacetamide	11095912	1
Caelo	Sulfacetamide	11085911	3
Caelo	Sulfacetamide	10145811	1
Caelo	Sulfacetamide	11085909	1
Caelo	Sulfacetamide	11085913	2
Caelo	Sulfacetamide	10145802	1
Caesar & Loretz GmbH	Sulfacetamide	15445902	2
EuRho/Phönix	Sulfacetamide	1702006-02	1
Euro OTC	Sulfacetamide	1312012-02	2
Euro OTC	Sulfacetamide	1509018-01	4
Euro OTC	Sulfacetamide	1702006-02	2
Euro OTC	Sulfacetamide	1808035-01	1
Euro OTC	Sulfacetamide	1112032-02	4
Euro OTC	Sulfacetamide	1509018-02	3
Euro OTC	Sulfacetamide	1702006-04	3
Euro OTC	Sulfacetamide	1702006-01	2
EuroRho 24.05.2013 Alli...	Sulfacetamide	1112032-02	2
Gehe	Sulfacetamide	1112032-01	4
Gehe	Sulfacetamide	11085904	1
Gehe	Sulfacetamide	1312012-01	2
Gehe	Sulfacetamide	1312012-02	1
Gehe	Sulfacetamide	1505025-01	1
Caelo	Sulfacetamide	1509018-02	2
Industrias GmbH / Ph	Sulfacetamide	64518	1
Phoenix	Sulfacetamide	15445904	1
Phoenix 17.02.2015	Sulfacetamide	1312012-02	2
Phönix	Sulfacetamide	11085910	1
Phönix 23.06.2014	Sulfacetamide	1312012-01	1
Phönix Gotha	Sulfacetamide	11085911	1
Phönix Gotha	Sulfacetamide	1312012-02	1

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Supplier	Substance	Batch	Spectra
Spangropharm	Sulfacetamide	11085915	1
Caelo	Sulfacetamide	15445901	1
Euro OTC	Sulfacetamide	1312012-01	4

- 111 176 spectra from 742 *Apo-Ident* customers from a total of 31 864 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sulfacetamide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sulfacetamide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	120	0	119 022
Type C	0	71	0	111 176

The substance/substance group *Sulfacetamide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 91.5493 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sulfacetamide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ciprofloxacin hydrochloride	34.08	—
Dequalinium chloride	47.91	—
Sodium cromoglicate	53.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sulfacetamide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20695	20695	0.00	24.48
21633	21902	5.77	27.21
21902	21902	0.00	27.41
23251	21902	7.21	28.15
23456	21902	5.26	25.63

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sulfadiazine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20753-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sulfadiazine; Sulfadiazinum

Special notes

When selecting the *Sulfadiazine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sulfadiazine	5	2	8

Second-stage model

For differentiation of the substance/substance group *Sulfadiazine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sulfadiazine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sulfadiazine	12164101	20753	40	1402053
Caelo	Sulfadiazine	13150011	21744	60	20130708
Caelo	Sulfadiazine	170566	23319	40	20170330*
Caelo	Sulfadiazine	17056602	23374	40	20170330
Caelo	Sulfadiazine	17056602	23447	40	20170330
Caelo	Sulfadiazine	191850	24735	40	20190730*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Sulfadiazine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 70 spectra of 2 reference samples from the substance/substance group *Sulfadiazine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sulfadiazine	172222	23630	30
Caelo	Sulfadiazine	190683	24523	40

- 119 072 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 11 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *Sulfadiazine*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sulfadiazine	17358901	1
Caelo	Sulfadiazine	17358905	2
Caelo	Sulfadiazine	17358910	3
Caelo	Sulfadiazine	17358917	1
Caelo	Sulfadiazine	13150004	1
Caelo	Sulfadiazine	17358906	1
Caelo	Sulfadiazine	11194204	1
Caesar & Loretz GmbH	Sulfadiazine	19068302	1

- 111 236 spectra from 742 *Apo-Ident* customers from a total of 31 883 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sulfadiazine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sulfadiazine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	70	0	119 072
Type C	0	11	0	111 236

The substance/substance group *Sulfadiazine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 91.4286 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sulfadiazine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Quinoline yellow	56.71	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sulfadiazine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20753	20753	0.00	97.04
21744	23319	2.45	96.62
23319	23319	0.00	95.99
23374	23319	2.28	96.47
23447	23319	1.21	95.57
24735	24735	0.00	98.26

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Sulfogaiacol hydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20327-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Sulfogaiacol hydrate; Potassium guaiacolsulfonate; Sulfoguaiacolum hydricum

Special notes

When selecting the *Sulfogaiacol hydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Sulfogaiacol hydrate	4	2	1

Second-stage model

For differentiation of the substance/substance group *Sulfogaiacol hydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Sulfogaiacol hydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Sulfogaiacol hyd. ...	13405805	21696	45	20140108
Caelo	Sulfogaiacol hyd. ...	190303	24495	40	20190222*
Gatt-Koller	Sulfogaiacol hyd. ...	1156/04152115	21843	60	20150410
Gatt-Koller	Sulfogaiacol hyd. ...	4543/01170317	23113	40	AR-17-FG-012520-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 185 spectra of 4 reference samples from the substance/substance group *Sulfogaiacol hydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 504 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Sulfogaiacol hydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Sulfogaiacol hydrate	170919	23300	40
Caelo	Sulfogaiacol hydrate	190921	24732	40
Caelo	Sulfogaiacol hydrate	170919	23306	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 12 spectra from 4 *Apo-Ident* customers from 1 batches from the substance/substance group *Sulfogaiacol hydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Sulfogaiacol hydrate	15343912	12

- 111 235 spectra from 742 *Apo-Ident* customers from a total of 31 890 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Sulfogaiacol hydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sulfogaiacol hydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	185	0	110 504
Type B	0	120	0	119 022
Type C	0	12	0	111 235

The substance/substance group *Sulfogaiacol hydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.7568 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sulfogaiacol hydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ciprofloxacin hydrochloride	66.63	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sulfogaiacol hydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21696	23113	8.23	75.92
21843	23113	8.23	77.17
23113	23113	0.00	76.09
24495	24495	0.00	60.82

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tannin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20018-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tannin; Tanninum

Special notes

When selecting the *Tannin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tannin	4	1	107

Second-stage model

For differentiation of the substance/substance group *Tannin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tannin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tannin	12336016	21608	60	20121127
Caelo	Tannin	172092	23631	40	20170829*
Fagron	Tannin	13H30-B03-287645	21653	60	1711482
Fagron	Tannin	16D08-B04-328410	23211	40	AR-17-FG-015963-01
Fagron	Tannin	16D08-B04-328410	23501	40	20160425

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Tannin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 40 spectra of 1 reference samples from the substance/substance group *Tannin*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tannin	16074504	23205	40

- 119 102 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 317 spectra from 197 *Apo-Ident* customers from 112 batches from the substance/substance group *Tannin*.
- Among them are spectra of independent samples from 105 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H.D.	Tannin	13E27-N08	1
ALH	Tannin	15091515	1
ALH	Tannin	14031919	1
Alliance Healthcare	Tannin	12336001	1
Caelo	Tannin	10019007	1
Caelo	Tannin	9128608	1
Caelo	Tannin	12171106	7
Caelo	Tannin	21101305	1
Caelo	Tannin	12336009	10
Caelo	Tannin	9128607	2
Caelo	Tannin	12336013	5
Caelo	Tannin	12336014	5
Caelo	Tannin	13031401	1
Caelo	Tannin	14031903	5
Caelo	Tannin	12336011	1
Caelo	Tannin	28011502	1
Caelo	Tannin	14031918	3
Caelo	Tannin	14031919	6
Caelo	Tannin	1509509	1
Caelo	Tannin	15091509	17
Caelo	Tannin	15091515	9
Caelo	Tannin	15F23-B01-326357	1
Caelo	Tannin	16D08-B04-334834	1
Caelo	Tannin	16074516	7
Caelo	Tannin	17343504	5
Caelo	Tannin	17343511	1
Caelo	Tannin	17343515	3
Caelo	Tannin	17343520	3
Caelo	Tannin	12336001	11
Caelo	Tannin	12336007	2
Caelo	Tannin	14031913	2
Caelo	Tannin	2211Q-01052	1
Caelo	Tannin	15091506	1
Caelo	Tannin	16074505	1
Caelo	Tannin	1524308	1
Caelo	Tannin	10315110	2
Caelo	Tannin	12171103	2

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Supplier	Substance	Batch	Spectra
Caelo	Tannin	14031901	2
Caelo	Tannin	14031905	3
Caelo	Tannin	16074509/171027T	1
Caelo	Tannin	1217112263904	1
Caelo	Tannin	15091503	2
Caelo	Tannin	17343503	1
Caelo	Tannin	18017701	3
Caelo	Tannin	10315107	2
Caelo	Tannin	12336005	2
Caelo	Tannin	15243802	3
Caelo	Tannin	17343505	1
Caelo	Tannin	16074509	7
Caelo	Tannin	4413I1052	1
Caelo	Tannin	19138203	1
Caelo	Tannin	12171101	4
Caelo	Tannin	12A27-N01	1
Caelo	Tannin	16D08-B04-328410	1
Caelo	Tannin	17343509	2
Caelo	Tannin	15243801	9
Caelo	Tannin	15091504	4
Caelo	Tannin	15091512	1
Caelo	Tannin	15091511	2
Caelo	Tannin	16074504	13
Caelo	Tannin	16074517	1
Caelo	Tannin	17343502	1
Caesar & Loretz GmbH	Tannin	17343509	1
Caesar & Loretz GmbH	Tannin	17343520	3
Caesar & Loretz GmbH / ...	Tannin	19138203	1
Caesar/Lorenz	Tannin	11302307	1
Caleo/Phoenix	Tannin	14K17-B08-306993	1
Ebert u. Jacobi 16.0...	Tannin	15091509	1
Fagron	Tannin	160300178B	3
Euro OTC	Tannin	16074509	1
Fagron	Tannin	160300029	1
Fagron	Tannin	11C09-N05	1
Fagron	Tannin	12E21-N04	4
Fagron	Tannin	12A27-N01	1
Fagron	Tannin	13H30-B03287645	1
Fagron	Tannin	160300126	1
Fagron	Tannin	14J06-B04-0858	1
Fagron	Tannin	14J06-B04	1
Fagron	Tannin	14e07-b03-298480	1
Fagron	Tannin	15F23-B01	1
Fagron	Tannin	16D08-B04-334834	3
Fagron	Tannin	16D08B04354470	1
Fagron	Tannin	1603001788	1
Fagron	Tannin	163001788	1
Fagron	Tannin	16D08-B04-354470	1
Fagron	Tannin	15F23-B01-326357	1
Fagron	Tannin	2212M-01052	1
Fagron	Tannin	13E27-N08	1
Fagron	Tannin	12H14N05	1
Fagron	Tannin	16D08-B04	1
Fagron	Tannin	16D08-B04-337161	1
Fagron	Tannin	12H14-N05	5
Fagron	Tannin	160300146	2
Fagron	Tannin	14E07-B03-298480	2
Fagron	Tannin	1014A-01052	1
Fagron	Tannin	13B28-N08	1
Fagron	Tannin	14J06-B04-299398	1

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Supplier	Substance	Batch	Spectra
Fagron	Tannin	15F23-B01-322984	2
Fagron	Tannin	16D08-b04	1
Fagron	Tannin	16D08B04335787	1
Fagron	Tannin	16D08-B04-335787	2
Fagron	Tannin	16D08-B04-352128	1
Fagron	Tannin	14A07-B01-293468	5
Fagron	Tannin	15F23B01326357	1
Fiebig	Tannin	16074518	1
Frago/Gehe	Tannin	15F23-B01	1
Gatt-Koller / Phoenix	Tannin	333508134613	2
Gatt-Koller / Phoenix	Tannin	3335/08134613	1
Gehe	Tannin	12171106	1
Gehe	Tannin	12H14-N05	1
Gehe	Tannin	12336016	2
Gehe	Tannin	16074504	1
Hirsch	Tannin	1811209	1
Caelo	Tannin	14031915	2
Euro OTC	Tannin	16074501	1
L10	Tannin	17343509	1
Nachprüfung	Tannin	5210A-01052	1
Noweda	Tannin	16074509	1
Caelo	Tannin	1236001	1
Caelo	Tannin	14031912	4
Phoenix	Tannin	12336013	1
phönix	Tannin	15/AKD65	1
phönix	Tannin	14E07-B03-293744	1
Phönix	Tannin	10315110	1
Phönix	Tannin	10313107Retest	1
Phönix	Tannin	17343520	1
Fagron	Tannin	14J06B04299398	1
Sanacorp	Tannin	12171102	1
Sanacorp	Tannin	12336011	1
Sanacorp	Tannin	12336014	1
Sanacorp	Tannin	14031912	1
Caelo	Tannin	16074518	6
Sanacorp WE: 26.01.15 E...	Tannin	14031912	1
Caelo	Tannin	11302307	5
Caelo	Tannin	14031920	2
Synopharm/Anzag	Tannin	3411I-01052	1
Caelo	Tannin	12336016	7
Caelo	Tannin		1
Fagron	Tannin	13H30-B03-287645	2
Fagron	Tannin	16D08-B04-328410	2
Sanacorp	Tannin		1

- 110930 spectra from 742 *Apo-Ident* customers from a total of 31780 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tannin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tannin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table

breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	40	0	119 102
Type C	0	314	3	110 930

The substance/substance group *Tannin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.0536 % (> 98.1073 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tannin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	33.51	—
Levothyroxin sodium	38.47	—
Oxytetracycline hydrochloride	45.20	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tannin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21608	21653	17.87	50.67
21653	21653	0.00	50.27
23211	23211	0.00	52.20
23501	23211	4.02	51.89
23631	23631	0.00	49.13

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tartaric acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20014-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tartaric acid; Acidum tartaricum

Special notes

When selecting the *Tartaric acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tartaric acid	6	3	127

Second-stage model

For differentiation of the substance/substance group *Tartaric acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tartaric acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tartaric acid	15130201	22383	60	20150416
Caelo	Tartaric acid	15164001	22384	60	1704461
Caelo	Tartaric acid	161468	22613	40	20160607*
Euro OTC	Tartaric acid	1907022	24806	40	20190813*
Fagron	Tartaric acid	13I25-B01-294093	22391	60	1711509
Fagron	Tartaric acid	14G07-B02-308554	22501	40	20140827

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 300 spectra of 6 reference samples from the substance/substance group *Tartaric acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 389 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 140 spectra of 3 reference samples from the substance/substance group *Tartaric acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tartaric acid	13217803	21457	60
Caelo	Tartaric acid	181212	24015	40
Fagron	Tartaric acid	14G07-B02-322976	23527	40

- 119 002 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 257 spectra from 131 *Apo-Ident* customers from 134 batches from the substance/substance group *Tartaric acid*.
- Among them are spectra of independent samples from 128 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
apomix	Tartaric acid	1111	1
Beiersdorf AG	Tartaric acid	11G19-N08	1
Caelo	Tartaric acid	12H02-n07	1
Caelo	Tartaric acid	15349105	8
Caelo	Tartaric acid	16260406	4
Caelo	Tartaric acid	12044101	2
Caelo	Tartaric acid	1169406	1
Caelo	Tartaric acid	12044103	4
Caelo	Tartaric acid	1204102	1
Caelo	Tartaric acid	12286903	2
Caelo	Tartaric acid	10180714	1
Caelo	Tartaric acid	12044119	3
Caelo	Tartaric acid	12286906	4
Caelo	Tartaric acid	9494239	1
Caelo	Tartaric acid	12240402	1
Caelo	Tartaric acid	12286904	2
Caelo	Tartaric acid	12240413	1
Caelo	Tartaric acid	17091402	1
Caelo	Tartaric acid	12286932	1
Caelo	Tartaric acid	15130205	2
Caelo	Tartaric acid	151302	1
Caelo	Tartaric acid	15164008	3
Caelo	Tartaric acid	13125-B01-294093	1
Caelo	Tartaric acid	15164010	1
Caelo	Tartaric acid	15130207	1
Caelo	Tartaric acid	15349101	3
Caelo	Tartaric acid	15349109	4
Caelo	Tartaric acid	14G07-B02-308555	2
Caelo	Tartaric acid	9041703	1
Caelo	Tartaric acid	16260404	5
Caelo	Tartaric acid	16260405	1
Caelo	Tartaric acid	8051809	1
Caelo	Tartaric acid	14186211	1
Caelo	Tartaric acid	17337504	2
Caelo	Tartaric acid	16146809	1

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Supplier	Substance	Batch	Spectra
Caelo	Tartaric acid	18121208	2
Caelo	Tartaric acid	17337505	3
Caelo	Tartaric acid	18121211	2
Caelo	Tartaric acid	1812104	1
Caelo	Tartaric acid	10199713	1
Caelo	Tartaric acid	12240415	1
Caelo	Tartaric acid	13116306	1
Caelo	Tartaric acid	13217806	2
Caelo	Tartaric acid	13116308	2
Caelo	Tartaric acid	14054521	1
Caelo	Tartaric acid	10180708	2
Caelo	Tartaric acid	12044102	3
Caelo	Tartaric acid	13B15-N01	2
Caelo	Tartaric acid	12286939	1
Caelo	Tartaric acid	18121204	3
Caelo	Tartaric acid	13116307	1
Caelo	Tartaric acid	10180713	2
Caelo	Tartaric acid	4110N-01053	1
Caelo	Tartaric acid	15349102	4
Caelo	Tartaric acid	17347103	3
Caelo	Tartaric acid	15349106	4
Caelo	Tartaric acid	17347104	2
Caelo	Tartaric acid	12286934	1
Caelo	Tartaric acid	15045304	1
Caelo	Tartaric acid	18121210	2
Caelo	Tartaric acid	18121201	1
Caelo	Tartaric acid	16260403	3
Caelo	Tartaric acid	15130206	1
Caelo	Tartaric acid	15349110	2
Caelo	Tartaric acid	13217807	1
Caelo	Tartaric acid	16146806	2
Caelo	Tartaric acid	15164002	3
Caelo	Tartaric acid	12286911	1
Caelo	Tartaric acid	14186213	4
Caelo	Tartaric acid	15045303	1
Caelo	Tartaric acid	12286924	1
Caesar & Loretz GmbH	Tartaric acid	18121204	1
Caesar & Loretz GmbH	Tartaric acid	18121211	1
Caesar & Loretz GmbH/An...	Tartaric acid	18121211	1
Caesar & Loretz GmbH/Ph...	Tartaric acid	17337505	1
Caesar & Loretz/ Noweda	Tartaric acid	12044103	1
canea, anzag	Tartaric acid	12286906	1
Distillerie Mazzari/Far...	Tartaric acid	13405	1
E-plus	Tartaric acid	15349107	1
Euro OTC	Tartaric acid	702265	1
Euro OTC	Tartaric acid	1604046-02	1
Fagron	Tartaric acid	1106211053	1
Fagron	Tartaric acid	11E24-N06	1
Fagron	Tartaric acid	20151112-2	1
Fagron	Tartaric acid	xxxxxxx	1
Fagron	Tartaric acid	12F18-N02	1
Fagron	Tartaric acid	2513M01053	1
Fagron	Tartaric acid	12K16-N02	1
Fagron	Tartaric acid	13B15-N01	8
Fagron	Tartaric acid	12H02-N07	3
Fagron	Tartaric acid	13I25-B01-285488	2
Fagron	Tartaric acid	12K29-B01-285247	1
Fagron	Tartaric acid	12225	1
Fagron	Tartaric acid	13I25-B01-285487	1
Fagron	Tartaric acid	15045303	1

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Supplier	Substance	Batch	Spectra
Fagron	Tartaric acid	14G07-B02-322976	1
Fagron	Tartaric acid	1325-B01-294094	1
Fagron	Tartaric acid	13G03-N14	1
Fagron	Tartaric acid	14G07-B02-322977	1
Fagron	Tartaric acid	14G07-802	1
Fagron	Tartaric acid	14G07-B02-330640	2
Fagron	Tartaric acid	13/25-B01	1
Fagron	Tartaric acid	1325-B01-294093	1
Fagron	Tartaric acid	12F18-No2	1
Fagron	Tartaric acid	14G07-B02	3
Fagron	Tartaric acid	13I25-B01-294095	1
Fagron	Tartaric acid	2414E1053	1
Fagron	Tartaric acid	13/25-B01-285488	2
Fagron	Tartaric acid	11E24-N060752/764	1
Fagron	Tartaric acid	13I25-B01-294094	3
Fagron	Tartaric acid	14519	1
Fagron	Tartaric acid	13I25-B01	1
Fagron	Tartaric acid	13I25-B01-285488	1
Fagron	Tartaric acid	12131	2
Fagron	Tartaric acid	13/25-B01-285487	1
Fagron	Tartaric acid	14186212	1
Fischar	Tartaric acid	704061	2
Fischar	Tartaric acid	705061	1
Fischar/Gehe	Tartaric acid	705061	1
Fischar/Phönix	Tartaric acid	704021	1
Fragon/Sanacorp	Tartaric acid	13G03-N14	2
Gatt-Koller / Phoenix	Tartaric acid	3334/08131514	1
Gehe	Tartaric acid	7284696	1
Gehe	Tartaric acid	703061	1
Gehe	Tartaric acid	1325-B01-285487	1
Gehe	Tartaric acid	16146806	1
GEHE 14.04.2014	Tartaric acid	12H02-N07	1
GEHE 14.04.2014	Tartaric acid	13G03-N14	2
Gehe/Fischer	Tartaric acid	706061	1
Gehe/Henry Lamotte	Tartaric acid	17/12	1
Klenk	Tartaric acid	13405	1
L12	Tartaric acid	14G07-B02-308555	1
Noweda 20.7.19	Tartaric acid	18121212	1
Noweda/ Fischar	Tartaric acid	702061	1
Otto Fischar	Tartaric acid	705061	2
Otto Fischar/ Gehe	Tartaric acid	709041	1
Otto Fischer GmbH	Tartaric acid	705061	1
Phoenix	Tartaric acid	12044115	1
Phoenix	Tartaric acid	12Ho2-N07	1
Phoenix	Tartaric acid	13116308	1
Phoenix	Tartaric acid	12K29B01	1
Fagron	Tartaric acid	13B15N01	1
Phönix	Tartaric acid	11e24-n06	1
Phönix	Tartaric acid	12286904	1
Phönix Gotha	Tartaric acid	704021	1
Sanacorp	Tartaric acid	17347104	1
Sanacorp WE: 19.0518 EK...	Tartaric acid	16260406	1
Caelo	Tartaric acid	11k10-n07	1
schubert / Phoenix	Tartaric acid	1014PLV-755	1
Spangropharm	Tartaric acid	10073111	1
Caelo	Tartaric acid	11169406	2
apomix	Tartaric acid		1
Caelo	Tartaric acid		1
Caelo	Tartaric acid	15164001	4
Caelo	Tartaric acid	15130201	6

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Supplier	Substance	Batch	Spectra
Fagron	Tartaric acid	14G07-B02-308554	3
Fagron	Tartaric acid	13I25-B01-294093	2

- 110 990 spectra from 742 *Apo-Ident* customers from a total of 31 759 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tartaric acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tartaric acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	300	0	110 389
Type B	0	140	0	119 002
Type C	0	252	5	110 990

The substance/substance group *Tartaric acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 99.8899 %)	98.0545 % (> 96.8872 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tartaric acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	33.04	—
Sodium tetraborate	34.80	—
Calcium lactate pentahydrate	40.09	—
Magnesium citrate	41.86	—
Oxalic acid	43.45	—
Menthol	47.31	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tartaric acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22384	22384	0.00	17.02
22501	22391	2.48	18.60
22613	22613	0.00	22.73
22383	22613	4.24	21.97
24806	24806	0.00	19.74
22391	22391	0.00	18.54

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Taurine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20403-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Taurine; Taurinum

Special notes

When selecting the *Taurine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Taurine	6	3	6

Second-stage model

For differentiation of the substance/substance group *Taurine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Taurine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Taurine	1306024-01	21108	50	20130822
Euro OTC	Taurine	1504032-01	21893	60	20150430
Euro OTC	Taurine	1504032-01	21992	60	9167
Euro OTC	Taurine	1602011	22370	60	20160218*
Euro OTC	Taurine	1607035	22795	40	20160819*
Euro OTC	Taurine	1704001	23177	40	20170426*
Euro OTC	Taurine	1904003	24632	40	20190425*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 350 spectra of 7 reference samples from the substance/substance group *Taurine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 339 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Taurine*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Taurine	1711006	23739	40
Euro OTC	Taurine	1810006	24310	40
Euro OTC	Taurine	1910017	24977	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 5 *Apo-Ident* customers from 6 batches from the substance/substance group *Taurine*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Taurine	1704001-01	2
el compra import	Taurine	1609025	1
elcompra	Taurine	xp17013244	1
Euro OTC	Taurine	1704001-01	1
Euro OTC	Taurine	XP16023196	1
hannes	Taurine	1202125	1
Gall Pharma / Phoenix	Taurine		1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 885 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Taurine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Taurine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	350	0	110 339
Type B	0	120	0	119 022
Type C	0	8	0	111 239

The substance/substance group *Taurine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2857 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Taurine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline chloride	46.95	–
Menthol	101.34	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Taurine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21108	21992	3.00	54.82
21893	21992	1.21	55.72
21992	21992	0.00	56.13
24632	24632	0.00	55.44
22370	22370	0.00	55.61
22795	22795	0.00	53.60
23177	23177	0.00	54.04

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Testosterone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20961-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Testosterone; Testosteronum

Special notes

When selecting the *Testosterone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Testosterone	11	12	67

Second-stage model

For differentiation of the substance/substance group *Testosterone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Testosterone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Testosterone	13406004	21370	50	20131219
Caelo	Testosterone	13406004	21371	50	20131219
Caelo	Testosterone	15244906	21987	60	20150814
Caelo	Testosterone	15244906	21987SI	38	20150814
Caelo	Testosterone	16311506	23244	40	20161123
Euro OTC	Testosterone	1307001-01	20961	40	1402309
Euro OTC	Testosterone	1511005	22232	60	20151119*
Euro OTC	Testosterone	1511005	22232SI	35	20151119*
Euro OTC	Testosterone	1604049	22561	40	20160510*
Euro OTC	Testosterone	1604049	22561SI	34	20160510*
Euro OTC	Testosterone	1910001	24963	40	20191024*
Euro OTC	Testosterone	1912017	25104	40	20191216*
Fagron	Testosterone	12F13-N02	20729	40	20120628
Fagron	Testosterone	15E18-B08-307772	21970	60	20150526
Fagron	Testosterone	15E18-B08-307772	21970SI	54	20150526
Fagron	Testosterone	17J26-B01-342032	23764	40	20171205

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 721 spectra of 16 reference samples from the substance/substance group *Testosterone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.
- 109968 spectra from a total of 1955 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Type B spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1126 spectra of 30 reference samples from the substance/substance group *Testosterone*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Testosterone	171199	23347	40
Caelo	Testosterone	181478	24265	40
Caelo	Testosterone	191113	24520	40
Euro OTC	Testosterone	1511005-01	21994	60
Euro OTC	Testosterone	1607013	22707	40
Euro OTC	Testosterone	1702017	23146	40
Euro OTC	Testosterone	1802015	23948	40
Euro OTC	Testosterone	1805006	24131	40
Euro OTC	Testosterone	1805021	24132	40
Euro OTC	Testosterone	1808033	24201	40
Euro OTC	Testosterone	1811027	24422	40
Euro OTC	Testosterone	1912014	24964	40
Caelo	Testosterone	16311506	23244SI [†]	30
Caelo	Testosterone	171199	23347SI	28
Caelo	Testosterone	171199	23670	40
Caelo	Testosterone	171199	23670SI	30
Caelo	Testosterone	181478	24265SI	40
Caelo	Testosterone	191113	24520SI	40
Euro OTC	Testosterone	1511005-01	21994SI	32
Euro OTC	Testosterone	1607013	22707SI	40
Euro OTC	Testosterone	1702017	23146SI	21
Euro OTC	Testosterone	1802015	23948SI	40
Euro OTC	Testosterone	1805006	24131SI	40
Euro OTC	Testosterone	1805021	24132SI	40
Euro OTC	Testosterone	1808033	24201SI	40
Euro OTC	Testosterone	1811027	24422SI	26
Euro OTC	Testosterone	1910001	24963SI [†]	39
Euro OTC	Testosterone	1912014	24964SI	30
Euro OTC	Testosterone	1912017	25104SI [†]	40
Fagron	Testosterone	17J26-B01-342032	23764SI [†]	30

- 118016 spectra from a total of 2404 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

- 191 spectra from 60 *Apo-Ident* customers from 74 batches from the substance/substance group *Testosterone*.
- Among them are spectra of independent samples from 67 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Testosterone	12176301	1
Audor Pharma	Testosterone	APZTSTG18003T	10
Audor Pharma	Testosterone	apztstg18004t	2
Audor Pharma	Testosterone	APZTST16001-M1T	1
Audor Pharma	Testosterone	AP5106061T	5
Audor Pharma	Testosterone	APZTSTG18004T	2
Caelo	Testosterone	13134804	1
Caelo	Testosterone	13134806	4
Caelo	Testosterone	13134808	1
Caelo	Testosterone	14201105	1
Caelo	Testosterone	14355605	1
Caelo	Testosterone	15412202	3
Caelo	Testosterone	17119902	2
Caelo	Testosterone	AP5106061T	1
Caelo	Testosterone	17119911	1
Caelo	Testosterone	17119903	1
Caelo	Testosterone	APZTSTG18004T	1
Caelo	Testosterone	18147810	1
Caelo	Testosterone	15195802	1
Caelo	Testosterone	19111302	1
Caelo	Testosterone	12176305	3
Caelo	Testosterone	16225804	2
Caelo	Testosterone	16225807	2
Caelo	Testosterone	APL00034466T	1
Caelo	Testosterone	15195803	1
Caelo	Testosterone	15412201	4
Caelo	Testosterone	18147803	1
Caelo	Testosterone	1604049-01	1
Caelo	Testosterone	11/07-N12	1
Caelo	Testosterone	1805021-01	1
Caesar & Loretz GmbH	Testosterone	18147803	1
Euro OTC	Testosterone	1511005-01	3
Euro OTC	Testosterone	1106011-03	4
Euro OTC	Testosterone	1404002-01	3
Euro OTC	Testosterone	1607013-01	1
Euro OTC	Testosterone	1607013-02	7
Euro OTC	Testosterone	1702017-01	40
Euro OTC	Testosterone	APZTSTG18003T	1
Euro OTC	Testosterone	1802015	1
Euro OTC	Testosterone	180506-01	1
Euro OTC	Testosterone	180500601	1
Euro OTC	Testosterone	1805021-01	7
Euro OTC	Testosterone	1811027-01	4
Euro OTC	Testosterone	18147813	2
Euro OTC	Testosterone	1811027	1
Euro OTC	Testosterone	1207005-02	1
Euro OTC	Testosterone	1106011-01	1
Euro OTC	Testosterone	3x1106011-03	1
Euro OTC	Testosterone	1106011-03	1
Euro OTC	Testosterone	1805006-01	1
Euro OTC	Testosterone	1808033-01	1
Euro OTC	Testosterone	1604049-01	3
Euro OTC	Testosterone	140400201	1
Euro OTC	Testosterone	1404002-1	1

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Supplier	Substance	Batch	Spectra
EUro/AHD	Testosterone	1106011-03	1
Euroo/Phoenix	Testosterone	1307001-01	1
Fagron	Testosterone	13I26-N08	1
Fagron	Testosterone	13g10n03	1
Fagron	Testosterone	13109b03294149	1
Fagron	Testosterone	13109b03298118	1
Fagron	Testosterone	13L09-B03-294148	1
Fagron	Testosterone	15E18-B08	1
Fagron	Testosterone	GTJ151103	1
Fagron	Testosterone	1712-B05	1
Fagron	Testosterone	17A12-B05-331496	1
Fagron	Testosterone	17J26-B01-342637	4
Fagron	Testosterone	13G10-N03	2
Fagron	Testosterone	17J26-B01-342033	2
Fagron	Testosterone	11/07-N12	1
Gehe	Testosterone	1811027-01	3
Gehe	Testosterone	1805021-01	1
GEHE	Testosterone	1912014-01	1
Haihang Industry	Testosterone	20140114-1	1
Haihang Industry	Testosterone	20140114-2	1
Noweda	Testosterone	1702017-01	1
Noweda	Testosterone	19111303	1
NWM CHina	Testosterone	TE150402	1
Phönix Gotha	Testosterone	1106011-03	1
Phönix Gotha	Testosterone	1408015-01	1
Shandong Northwest Manu...	Testosterone	GTJ160510	1
Spirig	Testosterone	13406003	1
Caelo	Testosterone	13406004	2
Caelo	Testosterone	15244906	1
Caelo	Testosterone	16311506	1
Caelo	Testosterone		1
Euro OTC	Testosterone	1307001-01	5
Fagron	Testosterone	12F13-N02	1

- 111 056 spectra from 742 *Apo-Ident* customers from a total of 31 818 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Testosterone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Testosterone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	721	0	109 968
Type B	0	1085	41	118 016
Type C	0	183	8	111 056

The substance/substance group *Testosterone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.1678 %)
Type B	100.0000 % (> 99.9893 %)	96.3588 % (> 96.0924 %)
Type C	100.0000 % (> 99.8899 %)	95.8115 % (> 94.2408 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Testosterone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prasterone	20.14	—
Estradiol valerate	39.70	—
Methylcellulose	43.72	—
Norethisterone acetate	45.02	—
Hydrocortisone	45.83	—
Menthol	48.22	—
Povidone iodine	54.36	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Testosterone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22561	22561	0.00	45.04
21970	22232	2.47	23.57
21987	22232	2.05	31.41
22232	22232	0.00	30.00
23244	22232	3.63	21.57
23764	22232	4.23	22.75
20729	24963	8.21	36.16
20961	20961	0.00	24.90
21370	22232	4.25	24.84
21371	22232	4.24	24.88
24963	24963	0.00	30.92
25104	25104	0.00	35.87

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Testosterone propionate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20880-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Testosterone propionate; Testosteroni propionas

Special notes

When selecting the *Testosterone propionate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Testosterone propionate	6	4	171

Second-stage model

For differentiation of the substance/substance group *Testosterone propionate* the following second-stage model is used:

- [Submodel 3](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Testosterone propionate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Testosterone pro...	12163607	20880	40	AR-15-FG-000623-01
Caelo	Testosterone pro...	15444709	23170	40	1707612
Euro OTC	Testosterone pro...	1109024-02	21644	60	1503607
Euro OTC	Testosterone pro...	1511003	22230	60	20151111*
Euro OTC	Testosterone pro...	1511003	22230SI	43	20151111*
Euro OTC	Testosterone pro...	1512023	22288	45	20151230*
Euro OTC	Testosterone pro...	1512023	22288SI	45	20151230*
Euro OTC	Testosterone pro...	2003011	25116	40	20200408*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 373 spectra of 8 reference samples from the substance/substance group *Testosterone propionate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 316 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 379 spectra of 10 reference samples from the substance/substance group *Testosterone propionate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Testosterone propionate	170963	23334	40
Caelo	Testosterone propionate	191986	24759	40
Euro OTC	Testosterone propionate	1710027	23734	40
Euro OTC	Testosterone propionate	1811040	24413	40
Caelo	Testosterone propionate	15444709	23170SI [†]	30
Caelo	Testosterone propionate	170963	23334SI	29
Caelo	Testosterone propionate	191986	24759SI	40
Euro OTC	Testosterone propionate	1710027	23734SI	40
Euro OTC	Testosterone propionate	1811040	24413SI	40
Euro OTC	Testosterone propionate	2003011	25116SI [†]	40

- 118763 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 452 spectra from 223 *Apo-Ident* customers from 179 batches from the substance/substance group *Testosterone propionate*.
- Among them are spectra of independent samples from 172 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Testosterone propionate	AP12E04-N01TP	1
AHD	Testosterone propionate	17325712	1
AHL	Testosterone propionate	APZTSP15003-MTP	2
Audor Pharma	Testosterone propionate	APZTSP1503-MTP	1
allianz	Testosterone propionate	15444704	1
Andor	Testosterone propionate	1109024-03TP	1
Anzag	Testosterone propionate	14L31-B02-304722	1
apomix	Testosterone propionate	13K25-B05-287648	1
Apomix / AHD	Testosterone propionate	40/14	1
Audor Pharma	Testosterone propionate	AP12J10-N08TP	2
Audor Pharma	Testosterone propionate	AP13K25-B05-287643TP	1
Audor Pharma	Testosterone propionate	APZTSP15003-MTP	13
Audor Pharma	Testosterone propionate	AP13K25-B05-287643T	1
Audor Pharma	Testosterone propionate	AP1109024-03	2
Audor Pharma	Testosterone propionate	AP12E04N01TP	2
Audor Pharma	Testosterone propionate	AP1109024-03TP	4
Caelo	Testosterone propionate	15444712	1
Caelo	Testosterone propionate	15444719	1
Caelo	Testosterone propionate	106212376	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Testosterone propionate	1108212376	1
Caelo	Testosterone propionate	612212376	1
Caelo	Testosterone propionate	903312376	1
Caelo	Testosterone propionate	12J10-N08	2
Caelo	Testosterone propionate	10235809	1
Caelo	Testosterone propionate	2013U-02376	1
Caelo	Testosterone propionate	12163612	6
Caelo	Testosterone propionate	1263607	1
Caelo	Testosterone propionate	13C08-N02	1
Caelo	Testosterone propionate	103004	1
Caelo	Testosterone propionate	15003008	2
Caelo	Testosterone propionate	15444705	3
Caelo	Testosterone propionate	15444707	4
Caelo	Testosterone propionate	15444711	1
Caelo	Testosterone propionate	15444706	3
Caelo	Testosterone propionate	15444710	5
Caelo	Testosterone propionate	1511003-01	1
Caelo	Testosterone propionate	15444717	1
Caelo	Testosterone propionate	23051816	1
Caelo	Testosterone propionate	17325711	1
Caelo	Testosterone propionate	17B09-B03-332376	1
Caelo	Testosterone propionate	16H22-B05-326483	1
Caelo	Testosterone propionate	15444714	3
Caelo	Testosterone propionate	13F05-N04	1
Caelo	Testosterone propionate	17325719	2
Caelo	Testosterone propionate	12163613	1
Caelo	Testosterone propionate	12163621	1
Caelo	Testosterone propionate	15444723	1
Caelo	Testosterone propionate	15169504	1
Caelo	Testosterone propionate	14L31-B02-304722	1
Caelo	Testosterone propionate	12A02-N05	1
Caelo	Testosterone propionate	19198603	1
Caelo	Testosterone propionate	12163619	2
Caelo	Testosterone propionate	14D15-B03-296959	1
Caelo	Testosterone propionate	15444718	1
Caelo	Testosterone propionate	12163616	4
Caelo	Testosterone propionate	13K25-B05-291974	1
Caelo	Testosterone propionate	15003002	8
Caelo	Testosterone propionate	15003004	3
Caelo	Testosterone propionate	15444702	5
Caelo	Testosterone propionate	36814m1	1
Caelo	Testosterone propionate	1710027-01	1
Caelo	Testosterone propionate	614E2376	1
Caelo	Testosterone propionate	151100301	1
Caelo	Testosterone propionate	15444713	1
Caelo	Testosterone propionate	15444721	2
Caelo	Testosterone propionate	17325717	2
Caelo	Testosterone propionate	17325716	1
Caelo	Testosterone propionate	19198604	1
Caelo	Testosterone propionate	15444703	13
Caelo	Testosterone propionate	16E24-B01-324711	1
Caelo	Testosterone propionate	17325707	8
Caelo	Testosterone propionate	18b06-B04	1
Caelo	Testosterone propionate	17325709	2
Caelo	Testosterone propionate	17325712	1
Caelo	Testosterone propionate	12163605	2
Caelo	Testosterone propionate	12163610	2
Caelo	Testosterone propionate	12163615	1
Caelo	Testosterone propionate	12163617	4
Caelo	Testosterone propionate	18B14-B02-353456	1

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Supplier	Substance	Batch	Spectra
Caelo	Testosterone propionate	36814M1	1
Caelo	Testosterone propionate	1109024-02	1
Caesar & Loretz GmbH	Testosterone propionate	17325717	1
Caesar & Loretz GmbH	Testosterone propionate	17325716	1
Caesar & Loretz GmbH/Ph...	Testosterone propionate	17325722	1
Ebert 17.08.16	Testosterone propionate	15444703	1
EuRho/Krieger	Testosterone propionate	1811040-01	3
Euro OTC	Testosterone propionate	1103010-02	1
Euro OTC	Testosterone propionate	1504023-01	2
Euro OTC	Testosterone propionate	1512023-01	2
Euro OTC	Testosterone propionate	18111709	1
Euro OTC	Testosterone propionate	15444718	2
Euro OTC	Testosterone propionate	1511003-01	7
Euro OTC	Testosterone propionate	1710027-01	3
Euro OTC	Testosterone propionate	1811040-01	3
Euro OTC	Testosterone propionate	970116/1	1
Euro OTC	Testosterone propionate	1103010-01	1
Euro/Lui	Testosterone propionate	1811040-01	1
Euro OTC	Testosterone propionate	1109024-03	1
Euro OTC	Testosterone propionate	1409037-01	2
Fagro/Noweda	Testosterone propionate	16H22-B05-326483	2
Fagron	Testosterone propionate	14A28-B12-296960	2
Fagron	Testosterone propionate	11C21-N09	1
Fagron	Testosterone propionate	6081201	1
Fagron	Testosterone propionate	12A02-N05	2
Fagron	Testosterone propionate	20121012-3	1
Fagron	Testosterone propionate	24411M1	1
Fagron	Testosterone propionate	13C08N02	1
Fagron	Testosterone propionate	3613M-02376	1
Fagron	Testosterone propionate	13F05-N04	16
Fagron	Testosterone propionate	14A28-B12-291977	1
Fagron	Testosterone propionate	36513M1	3
Fagron	Testosterone propionate	14A28-B12	2
Fagron	Testosterone propionate	14L31-B02	4
Fagron	Testosterone propionate	14L31-B02-304722	8
Fagron	Testosterone propionate	14A28-B12-296958	2
Fagron	Testosterone propionate	14L31B02304722	1
Fagron	Testosterone propionate	15K03-B03-315218	6
Fagron	Testosterone propionate	1501-B09-312867	1
Fagron	Testosterone propionate	14L31B02-304721	1
Fagron	Testosterone propionate	11G15-N07	1
Fagron	Testosterone propionate	16C24-B04-320784	3
Fagron	Testosterone propionate	15I01-B09-312867	1
Fagron	Testosterone propionate	15/01-B09	1
Fagron	Testosterone propionate	16E24B01322938	1
Fagron	Testosterone propionate	15I01-B01-318371	1
Fagron	Testosterone propionate	16E24-B01	1
Fagron	Testosterone propionate	16H22-B05-326483	6
Fagron	Testosterone propionate	16E24-B01-324711	1
Fagron	Testosterone propionate	16K24B03330544	1
Fagron	Testosterone propionate	17E22-B09	1
Fagron	Testosterone propionate	17J16-B03-344243	1
Fagron	Testosterone propionate	18B06-B04-352492	3
Fagron	Testosterone propionate	18/12-B03-355296	1
Fagron	Testosterone propionate	18b14-b02-353456	1
Fagron	Testosterone propionate	36814M1	2
Fagron	Testosterone propionate	18B06-B04-352493	3
Fagron	Testosterone propionate	14D15-B03-296959	4
Fagron	Testosterone propionate	18I12-B03-356702	1
Fagron	Testosterone propionate	17B09-B03-332376	3

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Supplier	Substance	Batch	Spectra
Fagron	Testosterone propionate	18B06-B04-351510	1
Fagron	Testosterone propionate	18/12-B03-356703	1
Fagron	Testosterone propionate	13/03-N02	1
Fagron	Testosterone propionate	11K18-N04	4
Fagron	Testosterone propionate	12E29-N02	1
Fagron	Testosterone propionate	12E04-N01	3
Fagron	Testosterone propionate	12J10-N08	4
Fagron	Testosterone propionate	14L31-B02-304721	8
Fagron	Testosterone propionate	13K25-B05	1
Fagron	Testosterone propionate	17B09-B04-335269	2
Fagron	Testosterone propionate	17j16-B03-341320	1
Fagron	Testosterone propionate	15K03-B-03-315218	1
Fagron	Testosterone propionate	11/12-N03	1
Fagron	Testosterone propionate	17J16-B03-341320	1
Fagron	Testosterone propionate	16H22-B05	2
Fagron	Testosterone propionate	13C08-N02	14
Fagron	Testosterone propionate	12C01-N01	1
Fagron	Testosterone propionate	13I03-N02	1
Fagron	Testosterone propionate	13K25-B05-291974	2
Fagron	Testosterone propionate	16H22-B05-326482	4
Fagron	Testosterone propionate	17J16-B04-346529	2
Fagron	Testosterone propionate	18B06-B04	1
Fagron	Testosterone propionate	18112-B03-356703	1
Fagron	Testosterone propionate	19K11-F05-366324	2
Fagron	Testosterone propionate	15D03-B02-310694	1
Fagron	Testosterone propionate	15k03-b03	1
Fagron	Testosterone propionate	15I01-B09-318371	1
Fagron	Testosterone propionate	17B09B03332376	1
Fagron	Testosterone propionate	17J16-B03	1
Fagron	Testosterone propionate	17J16B04346529	1
Fagron	Testosterone propionate	32012M1	1
Fagron	Testosterone propionate	10L03-N16	3
Fagron	Testosterone propionate	14A28B12296958	1
Fagron	Testosterone propionate	16E24B01324711	1
Fagron	Testosterone propionate	16K24-B03-330544	1
Fagron	Testosterone propionate	17E22-B09-338592	1
Fagron	Testosterone propionate	18B14-B02-353456	1
Fagron	Testosterone propionate	18I22-B03-356703	1
Fagron	Testosterone propionate	15/01-B09-318371	2
Fagron	Testosterone propionate	12/10-N08	1
Fagron	Testosterone propionate	12J10N-08	1
Fagron	Testosterone propionate	1511003-01	1
Fagron	Testosterone propionate	16E24-B01-322593	6
Fagron	Testosterone propionate	16E24-B01-325476	1
Fagron	Testosterone propionate	17J16-B03-343010	2
Fagron	Testosterone propionate	19K11-F05-366325	2
Fagron	Testosterone propionate	13K25-B05-287648	5
Fagron	Testosterone propionate	13K25B05287648	1
Fargon/Kehr	Testosterone propionate	17B09-B04-335269	1
Galderma	Testosterone propionate	15K03-B03-315218	1
Gatt-Koller	Testosterone propionate	606213811	1
Gatt-Koller	Testosterone propionate	3478/09153915	1
Gatt-Koller	Testosterone propionate	1803006	1
Gehe	Testosterone propionate	15444706	1
Gehe	Testosterone propionate	19H16-F03-364849	1
Gehe	Testosterone propionate	19K11-F05-366325	1
GEHE	Testosterone propionate	17325709	1
GEHE	Testosterone propionate	17325712	1
Gehe/Euro	Testosterone propionate	1200318/151100301	1
Fagron	Testosterone propionate	16H22B05326483	1

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Supplier	Substance	Batch	Spectra
Fagron	Testosterone propionate	17H25-B02-341321	3
Gehe/Fragon	Testosterone propionate	17B09B03332376	1
Fagron	Testosterone propionate	16C24B04320784	1
Infectopharm/Phönix	Testosterone propionate	18B06-B04-352493	1
Noweda	Testosterone propionate	12163610	1
Noweda	Testosterone propionate	1511003	1
Fagron	Testosterone propionate	13K25-B05-287647	9
phoenix	Testosterone propionate	12163615	1
Phoenix	Testosterone propionate	1109024-02	1
Phoenix/Cealo	Testosterone propionate	36814M1	1
Phönix	Testosterone propionate	13C08-N02	1
Phönix	Testosterone propionate	12J10-N08	1
Phönix	Testosterone propionate	12163617	1
Phönix	Testosterone propionate	12163613	1
Phönix	Testosterone propionate	13K25-B05	1
Phönix	Testosterone propionate	14L31-B02-304722	1
Phönix	Testosterone propionate	15444702	1
Phönix	Testosterone propionate	15444707	1
Phönix	Testosterone propionate	15444710	1
Phönix	Testosterone propionate	17325704	1
PHÖNIX	Testosterone propionate	15444720	1
Caelo	Testosterone propionate	12060102	2
Phönix WE:25.04.16 EK:1...	Testosterone propionate	14L31-B02-304722	1
Fagron	Testosterone propionate	12163616	2
Fagron	Testosterone propionate	18B06-B04-348557	1
Caelo	Testosterone propionate	17J16-B03-341320	1
Phönix/Euro	Testosterone propionate	110301002	1
Sanacorp	Testosterone propionate	14L31-B02-304721	2
Symbiotica Speciality	Testosterone propionate	15444702	2
Caelo	Testosterone propionate	15444709	1
Caelo	Testosterone propionate	12163607	1
Euro OTC	Testosterone propionate	1109024-02	1
	Testosterone propionate	16C24-B04-320784	2
Fagron	Testosterone propionate		1

- 110 795 spectra from 742 *Apo-Ident* customers from a total of 31 714 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Testosterone propionate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Testosterone propionate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	373	0	110 316
Type B	0	379	0	118 763
Type C	0	444	8	110 795

The substance/substance group *Testosterone propionate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3914 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.4169 %)
Type C	100.0000 % (> 99.8899 %)	98.2301 % (> 97.5664 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Testosterone propionate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Progesterone, micronized	6.49	41.14
Spironolactone	31.42	35.99
Povidone iodine	40.14	—
Estradiol valerate	40.36	—
Finasteride (form III)	40.93	—
Budesonide, micronized	42.12	—
Norethisterone acetate	46.18	—
⋮	⋮	⋮
Estriol	>50	79.09
Pregnenolone	>50	141.46
Alfatradiol	>50	163.28
Quinine hydrochloride	>50	344.70
Quinine sulfate	>50	410.49

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Testosterone propionate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22288	22288	0.00	8.38
21644	21644	0.00	8.76
20880	20880	0.00	6.87
25116	25116	0.00	7.27
23170	23170	0.00	6.49
22230	22230	0.00	9.09

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tetracaine base**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20947-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tetracaine base; Tetracainum

Special notes

When selecting the *Tetracaine base* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tetracaine base	7	9	80

Second-stage model

For differentiation of the substance/substance group *Tetracaine base* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tetracaine base*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tetracaine base	171117	23321	40	20170512*
Caelo	Tetracaine base	181249	24255	40	20180605*
Euro OTC	Tetracaine base	1405025-01	21603	60	AR-14-FG-012475-01
Euro OTC	Tetracaine base	1512022	22299	45	20160128*
Fagron	Tetracaine base	12L19-N10	20947	40	20130108
Fagron	Tetracaine base	14A16-B04-292915	21650	60	20140205
Fagron	Tetracaine base	14A16-B04-292916	21659	60	20140205

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 345 spectra of 7 reference samples from the substance/substance group *Tetracaine base*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 7 different batches.
- 110 344 spectra from a total of 1959 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 420 spectra of 10 reference samples from the substance/substance group *Tetracaine base*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Tetracaine base	1606009	22717	40
Euro OTC	Tetracaine base	1609010	22858	40
Euro OTC	Tetracaine base	1701035	23149	40
Euro OTC	Tetracaine base	1708024	23736	40
Euro OTC	Tetracaine base	1803002	24066	40
Euro OTC	Tetracaine base	1805019	24135	40
Euro OTC	Tetracaine base	1811021	24427	40
Euro OTC	Tetracaine base	1903004	24451	40
Euro OTC	Tetracaine base	1909021	24961	40
Fagron	Tetracaine base	14A16-B04-292915	21650 [†]	60

- 118 722 spectra from a total of 2410 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 229 spectra from 96 *Apo-Ident* customers from 89 batches from the substance/substance group *Tetracaine base*.
- Among them are spectra of independent samples from 79 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Tetracaine base	TC0091115	1
Caelo	Tetracaine base	T-290413-1	1
Caelo	Tetracaine base	14A16-B04	1
Caelo	Tetracaine base	1516B06312783	1
Caelo	Tetracaine base	16E23-B04	1
Caelo	Tetracaine base	17111706	5
Caelo	Tetracaine base	1805019-01	2
Caelo	Tetracaine base	17K13-B02-344448	1
Caelo	Tetracaine base	17K13-B02-347172	1
Caelo	Tetracaine base	16a13-b07-318736	1
Caelo	Tetracaine base	1811021-01	2
Caelo	Tetracaine base	16A13-B07-318736	5
Caelo	Tetracaine base	17111713	2
Caelo	Tetracaine base	1512022-01	1
Caelo	Tetracaine base	14A16-B04-292916	1
Caelo	Tetracaine base	1803002-01	1
Caelo	Tetracaine base	17111714	1
Caelo	Tetracaine base	14A16-B04-290207	1
Caelo	Tetracaine base	1701035-01	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Tetracaine base	17111705	1
Caelo	Tetracaine base	1606009-01	1
Caesar & Loretz GmbH	Tetracaine base	18124906	1
Ebert-Jacobi	Tetracaine base	16J12-B06-327371	1
Euro OTC	Tetracaine base	3081701	1
Euro OTC	Tetracaine base	10887133	1
Euro OTC	Tetracaine base	18041809	1
Euro OTC	Tetracaine base	1803002-01	7
Euro OTC	Tetracaine base	1903004-01	3
Euro OTC	Tetracaine base	1312034-01	6
Euro OTC	Tetracaine base	12081501	1
Euro OTC	Tetracaine base	151022-01	1
Euro OTC	Tetracaine base	160600-01	1
Euro OTC	Tetracaine base	160901	1
Euro OTC	Tetracaine base	1512022-01	2
Euro OTC	Tetracaine base	1708024-01	9
Euro OTC	Tetracaine base	1405025-02	1
Euro OTC	Tetracaine base	1701035-01	6
Euro/Noweda	Tetracaine base	1805019-01	2
Euro OTC	Tetracaine base	1606009-01	7
Euro OTC	Tetracaine base	1805019-01	4
Euro OTC	Tetracaine base	1609010-01	13
Euro OTC	Tetracaine base	1811021-01	14
Fagron	Tetracaine base	16A13-B07-322947	1
Fag	Tetracaine base	16A13-B07-322947	1
Fagron	Tetracaine base	11101-N09	1
Fagron	Tetracaine base	12F29-N05	7
Fagron	Tetracaine base	5111202	1
Fagron	Tetracaine base	12f29-n05	1
Fagron	Tetracaine base	12H23-N07	1
Fagron	Tetracaine base	11G12-N13	3
Fagron	Tetracaine base	3465093	1
Fagron	Tetracaine base	13D30-N11	2
Fagron	Tetracaine base	14A16-B04-290209	1
Fagron	Tetracaine base	14A16-B04-290208	3
Fagron	Tetracaine base	14G30-B08	2
Fagron	Tetracaine base	14A16-B04	1
Fagron	Tetracaine base	14G30-B08-297306	2
Fagron	Tetracaine base	14A16-B04-2490207	1
Fagron	Tetracaine base	14G30-B08-297307	1
Fagron	Tetracaine base	14g30-b08-297306	1
Fagron	Tetracaine base	14G30-B08-297305	1
Fagron	Tetracaine base	14K03-B02-303179	2
Fagron	Tetracaine base	14g30-b08-297305	1
Fagron	Tetracaine base	14K03-B02-303178	1
Fagron	Tetracaine base	14a16-b04-290208	1
Fagron	Tetracaine base	15/16-B06-312783	2
Fagron	Tetracaine base	1516-B06-316259	1
Fagron	Tetracaine base	1516-B06-316260	1
Fagron	Tetracaine base	16A13-B07-318736	4
Fagron	Tetracaine base	15G30-B04-312060	1
Fagron	Tetracaine base	15/16-B06-316260	1
Fagron	Tetracaine base	16E23-B04-323269	1
Fagron	Tetracaine base	16J12-B06	1
Fagron	Tetracaine base	16G29-B02-325570	1
Fagron	Tetracaine base	16G29-B02-325569	4
Fagron	Tetracaine base	17184083	1
Fagron	Tetracaine base	17K13-B02-347172	1
Fagron	Tetracaine base	TC0070716	1
Fagron	Tetracaine base	17K13-B02-344448	3

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Supplier	Substance	Batch	Spectra
Fagron	Tetracaine base	11L09-N03	3
Fagron	Tetracaine base	12F26-N05	1
Fagron	Tetracaine base	17E18-B02-337217	2
Fagron	Tetracaine base	2913Q-07165	1
Fagron	Tetracaine base	16J12-B06-329087	2
Fagron	Tetracaine base	TC0090913	2
Fagron	Tetracaine base	17E18-B02-337216	3
Fagron	Tetracaine base	14K03-B02	1
Fagron	Tetracaine base	11D07-N20	1
Fagron	Tetracaine base	16G29B02325570	2
Fagron	Tetracaine base	16J12-B06-327371	1
Fagron	Tetracaine base	14K03B02303178	1
Faron	Tetracaine base	15D01-B03-306258	2
Gehe	Tetracaine base	1805019-01	2
Gehe	Tetracaine base	1811021-01	1
GEHE	Tetracaine base	16G29-B02-325569	1
GEHE	Tetracaine base	18C26-B01	1
GEHE 02.05.2014	Tetracaine base	14A16-B04-290208	2
GEHE 04.05	Tetracaine base	1405025-01	1
Hepart	Tetracaine base	15G30-B04-310590	1
Noweda	Tetracaine base	19A15-B01-361269	3
Fagron	Tetracaine base	15D01-B03-306258	1
Noweda/Fargon	Tetracaine base	16/12-B06-329087	1
Phoenix	Tetracaine base	3118	1
Phoenix	Tetracaine base	1811021-01	1
Phoenix 07.10.14	Tetracaine base	14A16-B04-292916	1
Phoenix Goettin	Tetracaine base	14G30-B08-297306	1
Phönix	Tetracaine base	11g12-n13	1
Phönix	Tetracaine base	3465093	1
Phönix	Tetracaine base	1303018-01	1
Phönix	Tetracaine base	1312034-01	2
Rondell Apotheke	Tetracaine base	1312034-01	1
Euro OTC	Tetracaine base	1405025-01	1
Fagron	Tetracaine base	12L19-N10	5
Fagron	Tetracaine base	14A16-B04-292916	1
Fagron	Tetracaine base		1

- 111 018 spectra from 742 *Apo-Ident* customers from a total of 31 803 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tetracaine base* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tetracaine base* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	345	0	110 344
Type B	0	391	29	118 722
Type C	0	226	3	111 018

The substance/substance group *Tetracaine base* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2609 %)
Type B	100.0000 % (> 99.9893 %)	93.0952 % (> 92.3810 %)
Type C	100.0000 % (> 99.8899 %)	98.6900 % (> 97.3799 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tetracaine base* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Estriol	65.55	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tetracaine base* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20947	21603	2.41	67.84
21603	21603	0.00	67.19
21650	22299	2.35	66.84
21659	21603	3.36	68.83
22299	22299	0.00	65.55
23321	23321	0.00	68.00
24255	24255	0.00	66.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tetracaine hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20037-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tetracaine hydrochloride; Tetracaini hydrochloridum

Special notes

When selecting the *Tetracaine hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tetracaine hydrochloride	8	11	230

Second-stage model

For differentiation of the substance/substance group *Tetracaine hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tetracaine hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tetracaine hydro...	12019822	20924	40	20120228
Caelo	Tetracaine hydro...	15437108	23163	40	20160211
Euro OTC	Tetracaine hydro...	1506040	21845	60	20150713*
Euro OTC	Tetracaine hydro...	1512019	22285	45	20151228*
Euro OTC	Tetracaine hydro...	1612005	22912	40	20170112*
Euro OTC	Tetracaine hydro...	1807017	24141	40	20180730*
Fagron	Tetracaine hydro...	15K04-B03-322151	23162	40	20160112
Fagron	Tetracaine hydro...	16G28-B03-327368	23500	40	20160826

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 345 spectra of 8 reference samples from the substance/substance group *Tetracaine hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 344 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 440 spectra of 11 reference samples from the substance/substance group *Tetracaine hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tetracaine hydrochloride	190119	24561	40
Euro OTC	Tetracaine hydrochloride	1607031	22708	40
Euro OTC	Tetracaine hydrochloride	1706018	23558	40
Euro OTC	Tetracaine hydrochloride	1712012	23886	40
Euro OTC	Tetracaine hydrochloride	1310006	23910	40
Euro OTC	Tetracaine hydrochloride	1803001	24079	40
Euro OTC	Tetracaine hydrochloride	1812006	24448	40
Euro OTC	Tetracaine hydrochloride	1902015	24452	40
Euro OTC	Tetracaine hydrochloride	1907007	24783	40
Euro OTC	Tetracaine hydrochloride	1909024	24974	40
Euro OTC	Tetracaine hydrochloride	2001011	25105	40

- 118 702 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 1003 spectra from 346 *Apo-Ident* customers from 239 batches from the substance/substance group *Tetracaine hydrochloride*.
- Among them are spectra of independent samples from 230 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Tetracaine hydrochloride	15A12-B03-308857	1
AHD	Tetracaine hydrochloride	15437121	1
AHD	Tetracaine hydrochloride	18060602	1
AHD	Tetracaine hydrochloride	18060614	1
Fagron	Tetracaine hydrochloride	13K25-Bo4-290276	1
Fagron	Tetracaine hydrochloride	1607031-01	1
Alliance Health	Tetracaine hydrochloride	14C18-B03-293967	1
Alliance Health 05.05.2...	Tetracaine hydrochloride	13H21-B02-286559	1
Alliance Health 22.08.2...	Tetracaine hydrochloride	6093549	1
Alliance Health 30.04.2...	Tetracaine hydrochloride	1303012-01	2
Alliance Healthcare	Tetracaine hydrochloride	12H24-N05	1
Anzag	Tetracaine hydrochloride	1411019-01	1
Anzag	Tetracaine hydrochloride	14710369	1
Anzag	Tetracaine hydrochloride	17256705	1
Euro OTC	Tetracaine hydrochloride	1310006-02	1
BASF Fine Chemicals Swi...	Tetracaine hydrochloride	13155714	1
BASF Pharma	Tetracaine hydrochloride	1411019-01	1
BASF Pharma S.A.	Tetracaine hydrochloride	1310006-01	1
BASF Pharma S.A.	Tetracaine hydrochloride	1409026-02	1
Bomastus / Alliance Hea...	Tetracaine hydrochloride	16G28-B03-327368	2
Bombastus	Tetracaine hydrochloride	13H21-B02-286558	1
Bombastus	Tetracaine hydrochloride	1712012-01	2

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Supplier	Substance	Batch	Spectra
Caelo	Tetracaine hydrochloride	10118211	1
Caelo	Tetracaine hydrochloride	1110010-02	2
Caelo	Tetracaine hydrochloride	10118210	2
Caelo	Tetracaine hydrochloride	12019812	3
Caelo	Tetracaine hydrochloride	12019810	5
Caelo	Tetracaine hydrochloride	12019816	11
Caelo	Tetracaine hydrochloride	12019815	1
Caelo	Tetracaine hydrochloride	27111305	1
Caelo	Tetracaine hydrochloride	13155705	3
Caelo	Tetracaine hydrochloride	1310006-01	1
Caelo	Tetracaine hydrochloride	13155716	2
Caelo	Tetracaine hydrochloride	15079501	2
Caelo	Tetracaine hydrochloride	13155727	6
Caelo	Tetracaine hydrochloride	13155703	1
Caelo	Tetracaine hydrochloride	14C18-B03-300200	1
Caelo	Tetracaine hydrochloride	14C18-B03-300199	1
Caelo	Tetracaine hydrochloride	14G14-B08-300198	1
Caelo	Tetracaine hydrochloride	15196102	5
Caelo	Tetracaine hydrochloride	15356902	2
Caelo	Tetracaine hydrochloride	15437102	1
Caelo	Tetracaine hydrochloride	150604002	1
Caelo	Tetracaine hydrochloride	15437107	2
Caelo	Tetracaine hydrochloride	15437109	10
Caelo	Tetracaine hydrochloride	1537109	1
Caelo	Tetracaine hydrochloride	1607031-01	7
Caelo	Tetracaine hydrochloride	1110010-07	1
Caelo	Tetracaine hydrochloride	15437117	4
Caelo	Tetracaine hydrochloride	1508040-01	1
Caelo	Tetracaine hydrochloride	170601801	1
Caelo	Tetracaine hydrochloride	15437120	1
Caelo	Tetracaine hydrochloride	17256705	6
Caelo	Tetracaine hydrochloride	17256703	2
Caelo	Tetracaine hydrochloride	18060603	2
Caelo	Tetracaine hydrochloride	17114181	1
Caelo	Tetracaine hydrochloride	18060610	1
Caelo	Tetracaine hydrochloride	18060612	3
Caelo	Tetracaine hydrochloride	18060614	2
Caelo	Tetracaine hydrochloride	12019802	4
Caelo	Tetracaine hydrochloride	1712012-01	2
Caelo	Tetracaine hydrochloride	1803001-01	7
Caelo	Tetracaine hydrochloride	1805019-01	1
Caelo	Tetracaine hydrochloride	12H24-N05	1
Caelo	Tetracaine hydrochloride	13155720	2
Caelo	Tetracaine hydrochloride	9070003	2
Caelo	Tetracaine hydrochloride	15437104	13
Caelo	Tetracaine hydrochloride	19011908	1
Caelo	Tetracaine hydrochloride	15437114	9
Caelo	Tetracaine hydrochloride	6093549	1
Caelo	Tetracaine hydrochloride	19011901	3
Caelo	Tetracaine hydrochloride	1313012-01	1
Caelo	Tetracaine hydrochloride	1411019-01	4
Caelo	Tetracaine hydrochloride	13155706	10
Caelo	Tetracaine hydrochloride	13155724	4
Caelo	Tetracaine hydrochloride	15196103	6
Caelo	Tetracaine hydrochloride	16G28-B03-332099	2
Caelo	Tetracaine hydrochloride	1405026-01	1
Caelo	Tetracaine hydrochloride	13K25-B04-290276	1
Caelo	Tetracaine hydrochloride	259/22	1
Caelo	Tetracaine hydrochloride	150604001	1
Caelo	Tetracaine hydrochloride	1512019-01	2

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Supplier	Substance	Batch	Spectra
Caelo	Tetracaine hydrochloride	15079507	1
Caelo	Tetracaine hydrochloride	14c18-b03-293966	1
Caelo	Tetracaine hydrochloride	15437122	3
Caelo	Tetracaine hydrochloride	1310006-02	1
Caelo	Tetracaine hydrochloride	10118225	4
Caelo	Tetracaine hydrochloride	17256704	2
Caelo	Tetracaine hydrochloride	1706018-01	1
Caelo	Tetracaine hydrochloride	15437119	12
Caelo	Tetracaine hydrochloride	18060602	15
Caelo	Tetracaine hydrochloride	18060620	5
Caelo	Tetracaine hydrochloride	1207001-01	1
Caelo	Tetracaine hydrochloride	15437106	2
Caelo	Tetracaine hydrochloride	15K04-B03-318368	2
Caelo	Tetracaine hydrochloride	1512019-02	1
Caelo	Tetracaine hydrochloride	16G25-B03-332099	1
Caelo	Tetracaine hydrochloride	15196104	2
Caelo	Tetracaine hydrochloride	15K04-B03-318369	1
Caelo	Tetracaine hydrochloride	161200501	1
Caelo	Tetracaine hydrochloride	1409026-02	3
Caelo	Tetracaine hydrochloride	15437121	7
Caelo	Tetracaine hydrochloride	18060604	1
Caelo	Tetracaine hydrochloride	18060609	1
Caelo	Tetracaine hydrochloride	12019820	1
Caelo	Tetracaine hydrochloride	13155714	2
Caelo	Tetracaine hydrochloride	1612005-01	1
Caelo	Tetracaine hydrochloride	17G03-B07-345008	2
Caelo	Tetracaine hydrochloride	15H24-B03-311450	1
Caelo	Tetracaine hydrochloride	13155711	7
Caelo	Tetracaine hydrochloride	14G14-B08	1
Caesar & Loretz	Tetracaine hydrochloride	1803001-01	1
Caesar & Loretz GmbH	Tetracaine hydrochloride	18060621	1
Caesar & Loretz GmbH	Tetracaine hydrochloride	19011901	4
Caesar & Loretz GmbH	Tetracaine hydrochloride	19011903	1
Caesar & Loretz GmbH/Kr...	Tetracaine hydrochloride	19011908	2
Calo/AHD	Tetracaine hydrochloride	13155727	1
Ebert-Jacobi	Tetracaine hydrochloride	1612005-01	1
Ebert-Jacobi	Tetracaine hydrochloride	15K04-B03-328163	1
EuRho	Tetracaine hydrochloride	1110010-01	2
EuRho	Tetracaine hydrochloride	2906009V-04	1
EuRho	Tetracaine hydrochloride	1106035-01	2
EuRho	Tetracaine hydrochloride	1615I-02039	1
EuRho	Tetracaine hydrochloride	1712012-01	1
EuRho Anzag	Tetracaine hydrochloride	1207001-01	1
Euro OTC	Tetracaine hydrochloride	1607031-01	34
EuRho/	Tetracaine hydrochloride	1712012-01	2
EuRho/ Phönix	Tetracaine hydrochloride	1612002-01	1
Euro	Tetracaine hydrochloride	1506040-01	1
Euro CT Phönix	Tetracaine hydrochloride	1207001-02	1
Euro OT/Phönix	Tetracaine hydrochloride	TH0030315	1
Euro OTC	Tetracaine hydrochloride	1110010-02	6
Euro OTC	Tetracaine hydrochloride	20160812-2	1
Euro OTC	Tetracaine hydrochloride	2906009V-03	1
Euro OTC	Tetracaine hydrochloride	1207001-02	8
Euro OTC	Tetracaine hydrochloride	130301201	1
Euro OTC	Tetracaine hydrochloride	1405026-01	17
Euro OTC	Tetracaine hydrochloride	14090-26	1
Euro OTC	Tetracaine hydrochloride	14G14-B08-300202	1
Euro OTC	Tetracaine hydrochloride	140902601	1
Euro OTC	Tetracaine hydrochloride	141101901	1
Euro OTC	Tetracaine hydrochloride	1409026-02	10

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Supplier	Substance	Batch	Spectra
Euro OTC	Tetracaine hydrochloride	140902602	1
Euro OTC	Tetracaine hydrochloride	3113M-02039	1
Euro OTC	Tetracaine hydrochloride	1512019-01	29
Euro OTC	Tetracaine hydrochloride	10416THCL	1
Euro OTC	Tetracaine hydrochloride	1106035	1
Euro OTC	Tetracaine hydrochloride	1512019-02	1
Euro OTC	Tetracaine hydrochloride	1612005-015445	1
Euro OTC	Tetracaine hydrochloride	21071807	1
Euro OTC	Tetracaine hydrochloride	1803001	1
Euro OTC	Tetracaine hydrochloride	1909024-01	3
Euro OTC	Tetracaine hydrochloride	1902012-01	1
Euro OTC	Tetracaine hydrochloride	13155710	4
Euro OTC	Tetracaine hydrochloride	1907007-01	1
Euro OTC	Tetracaine hydrochloride	1603026-01	1
Euro OTC	Tetracaine hydrochloride	TH0030315	1
Euro OTC	Tetracaine hydrochloride	150604001	1
Euro OTC	Tetracaine hydrochloride	6093547	1
Euro OTC	Tetracaine hydrochloride	11110010-02	1
Euro OTC	Tetracaine hydrochloride	24102014A	1
Euro OTC	Tetracaine hydrochloride	17081503	1
Euro OTC	Tetracaine hydrochloride	1506040-01	28
Euro OTC	Tetracaine hydrochloride	15120019-01	1
Euro OTC	Tetracaine hydrochloride	151-2019-01	1
Euro OTC	Tetracaine hydrochloride	3071716	1
Euro OTC	Tetracaine hydrochloride	180300101	5
Euro OTC	Tetracaine hydrochloride	1303012-01	21
Euro OTC	Tetracaine hydrochloride	1411019-01	24
Euro OTC	Tetracaine hydrochloride	1405026-04	3
Euro OTC	Tetracaine hydrochloride	1607031	1
Euro OTC	Tetracaine hydrochloride	1902015-01	4
Euro OTC	Tetracaine hydrochloride	1803001-01	22
Euro OTC	Tetracaine hydrochloride	1807017-01	5
Euro OTC	Tetracaine hydrochloride	1712012-01	16
Euro OTC	Tetracaine hydrochloride	1409026-01	12
Euro OTC	Tetracaine hydrochloride	TH0070816	1
Euro OTC	Tetracaine hydrochloride	1706018-01	17
Euro OTC	Tetracaine hydrochloride	1803001-1	1
Euro OTC	Tetracaine hydrochloride	1506040-02	7
Euro OTC	Tetracaine hydrochloride	1612005-01	26
Euro OTC	Tetracaine hydrochloride	1110010-01	5
Euro OTC	Tetracaine hydrochloride	181200601	1
Euro OTC	Tetracaine hydrochloride	180701701	1
Euro OTC	Tetracaine hydrochloride	4811A-02039	1
Euro OTC	Tetracaine hydrochloride	160703101	2
Euro OTC	Tetracaine hydrochloride	170323181	1
Euro OTC	Tetracaine hydrochloride	161200501	2
Euro OTC	Tetracaine hydrochloride	1409026	1
Euro OTC	Tetracaine hydrochloride	1310006-01	18
Euro OTC	Tetracaine hydrochloride	1405026-02	1
Euro OTC	Tetracaine hydrochloride	1607032-01	1
Euro OTC	Tetracaine hydrochloride	1106035-01	1
Euro OTG	Tetracaine hydrochloride	1207001-01	1
Euro OTG Pharma	Tetracaine hydrochloride	1409026-02	1
Euro OTG/ AHD	Tetracaine hydrochloride	1706018-01	2
Euro/Phönix	Tetracaine hydrochloride	1506040-01	1
euroct/gehe	Tetracaine hydrochloride	1405026-01	1
Euro OTC	Tetracaine hydrochloride	1902015	1
Euro OTC	Tetracaine hydrochloride	5016Y-02039	1
Euro OTC	Tetracaine hydrochloride	1404026-02	1
Euro OTC	Tetracaine hydrochloride	1207001-01	8

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Supplier	Substance	Batch	Spectra
Euro OTC	Tetracaine hydrochloride	1812006-01	8
EuroTOC / Noweda	Tetracaine hydrochloride	131000601	2
Fagro/Gehe	Tetracaine hydrochloride	16G28-B03-327368	2
Fagron	Tetracaine hydrochloride	14C18-B03-300199	4
Fagron	Tetracaine hydrochloride	14C18-B03-293967	1
Fagron	Tetracaine hydrochloride	12C22-N04	5
Fagron	Tetracaine hydrochloride	11C22-N04	1
Fagron	Tetracaine hydrochloride	12H-N05	1
Fagron	Tetracaine hydrochloride	13D11-N07	11
Fagron	Tetracaine hydrochloride	3913I-02039	1
Fagron	Tetracaine hydrochloride	4313E-02039	1
Fagron	Tetracaine hydrochloride	11/15-N12	1
Fagron	Tetracaine hydrochloride	13D11-N01	1
Fagron	Tetracaine hydrochloride	212131/221630-0002	1
Fagron	Tetracaine hydrochloride	13G02-N01	1
Fagron	Tetracaine hydrochloride	6093547	2
Fagron	Tetracaine hydrochloride	13K25-B04-290276	2
Fagron	Tetracaine hydrochloride	13K25-B04290276	1
Fagron	Tetracaine hydrochloride	13H21-B02-286559	1
Fagron	Tetracaine hydrochloride	13155711	1
Fagron	Tetracaine hydrochloride	10990834	3
Fagron	Tetracaine hydrochloride	13K25-B04	1
Fagron	Tetracaine hydrochloride	14c18d03300199	1
Fagron	Tetracaine hydrochloride	13K25-B04-290278	1
Fagron	Tetracaine hydrochloride	13k25-b04-290276	1
Fagron	Tetracaine hydrochloride	10990837	3
Fagron	Tetracaine hydrochloride	10330837	1
Fagron	Tetracaine hydrochloride	14C18-B03-300200	4
Fagron	Tetracaine hydrochloride	15A12-B03-308857	7
Fagron	Tetracaine hydrochloride	14C18-B03-300200	1
Fagron	Tetracaine hydrochloride	10990841	2
Fagron	Tetracaine hydrochloride	14C18-B03	1
Fagron	Tetracaine hydrochloride	15H24-B03	3
Fagron	Tetracaine hydrochloride	15H24-B03-313594	5
Fagron	Tetracaine hydrochloride	15h24-b03-313594	1
Fagron	Tetracaine hydrochloride	13509149	1
Fagron	Tetracaine hydrochloride	15K04B03318369	1
Fagron	Tetracaine hydrochloride	15K04-B03-318368	3
Fagron	Tetracaine hydrochloride	15K04-b03-312151	1
Fagron	Tetracaine hydrochloride	16G28-B03-330363	1
Fagron	Tetracaine hydrochloride	218I-02039	1
Fagron	Tetracaine hydrochloride	17G03-B07	4
Fagron	Tetracaine hydrochloride	17G05-B04-341204	1
Fagron	Tetracaine hydrochloride	17114181	7
Fagron	Tetracaine hydrochloride	17G03-B07-341853	3
Fagron	Tetracaine hydrochloride	15K04-B03-318369	1
Fagron	Tetracaine hydrochloride	18J03-B05-356329	2
Fagron	Tetracaine hydrochloride	TH0100718	3
Fagron	Tetracaine hydrochloride	17G03-B07-341853	1
Fagron	Tetracaine hydrochloride	16G8-B03-327368	1
Fagron	Tetracaine hydrochloride	13H21-B02-286558	3
Fagron	Tetracaine hydrochloride	12H24-N050696/1050	1
Fagron	Tetracaine hydrochloride	16G28-B03-327369	2
Fagron	Tetracaine hydrochloride	12K01-N04	7
Fagron	Tetracaine hydrochloride	1303012-01	1
Fagron	Tetracaine hydrochloride	15H24-B03-311450	6
Fagron	Tetracaine hydrochloride	18J03-B05-359814	1
Fagron	Tetracaine hydrochloride	16G28-B03-334124	2
Fagron	Tetracaine hydrochloride	17G03-B07-338540	1
Fagron	Tetracaine hydrochloride	17G03-B07-341319	1

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Supplier	Substance	Batch	Spectra
Fagron	Tetracaine hydrochloride	17G03-B07-349368	1
Fagron	Tetracaine hydrochloride	11A31-N15	1
Fagron	Tetracaine hydrochloride	10A29-N12	2
Fagron	Tetracaine hydrochloride	6093549	1
Fagron	Tetracaine hydrochloride	18J03-B05-358080	2
Fagron	Tetracaine hydrochloride	13H21-B02	2
Fagron	Tetracaine hydrochloride	17G03-B07-338538	6
Fagron	Tetracaine hydrochloride	14C18-B03-293966	7
Fagron	Tetracaine hydrochloride	12H24-N05	11
Fagron	Tetracaine hydrochloride	3413U02039	1
Fagron	Tetracaine hydrochloride	13K25B04290277	1
Fagron	Tetracaine hydrochloride	14G14B08300198	1
Fagron	Tetracaine hydrochloride	14710369	1
Fagron	Tetracaine hydrochloride	16G28-B03-330362	2
Fagron	Tetracaine hydrochloride	17G03-B07-345009	1
Fagron	Tetracaine hydrochloride	17G03-B07-351509	2
Fagron	Tetracaine hydrochloride	18J03-B05-356330	1
Fagron	Tetracaine hydrochloride	18J03-B05-361979	1
Fagron	Tetracaine hydrochloride	1506040-02	1
Fagron	Tetracaine hydrochloride	17G03-B07-338539	2
Fagron	Tetracaine hydrochloride	1803001-01	1
Fagron	Tetracaine hydrochloride	1418-03-300199	1
Fargon Services NL	Tetracaine hydrochloride	15K04-B03-322151	5
Fargon/AllianceH.	Tetracaine hydrochloride	17G03-B07-338538	1
Fiebig/Calo	Tetracaine hydrochloride	17256704	1
Finze	Tetracaine hydrochloride	2906009-02	1
Gatt-Koller	Tetracaine hydrochloride	1803034	2
Gatt-Koller	Tetracaine hydrochloride	KNC1825J18	1
Gatt-Koller	Tetracaine hydrochloride	1900461	6
Gatt-Koller / Phoenix	Tetracaine hydrochloride	80/02140614	2
Gehe	Tetracaine hydrochloride	1310006-01	1
Gehe	Tetracaine hydrochloride	13155711	2
Gehe	Tetracaine hydrochloride	15K04-B03-322151	1
Gehe	Tetracaine hydrochloride	1812006-01	1
Gehe	Tetracaine hydrochloride	1902015-01	1
Gehe	Tetracaine hydrochloride	1909024-01	1
GEHE	Tetracaine hydrochloride	1612005-01	1
GEHE	Tetracaine hydrochloride	1706018-01	1
GEHE	Tetracaine hydrochloride	18060602	2
GEHE	Tetracaine hydrochloride	17G03-B07-338540	1
GEHE	Tetracaine hydrochloride	18060614	2
Caelo	Tetracaine hydrochloride	18060621	3
Gehe 07.07.2014	Tetracaine hydrochloride	13155706	1
Caelo	Tetracaine hydrochloride	1260917/15437119	1
Gutenberg-Apotheke	Tetracaine hydrochloride	13D11-N07	1
Jenne	Tetracaine hydrochloride	13D11-No7	1
Euro OTC	Tetracaine hydrochloride	18701701	1
Fagron	Tetracaine hydrochloride	16G2-B03-327368	1
Noveda	Tetracaine hydrochloride	12H24-N05	1
Noveda	Tetracaine hydrochloride	1106035-01	2
Noveda	Tetracaine hydrochloride	120700-02	1
Noveda	Tetracaine hydrochloride	1310006-01	1
Noveda	Tetracaine hydrochloride	14G14-B08	1
Noveda/ BASF Pharma (Ev...	Tetracaine hydrochloride	12H24-N05	1
Fagron	Tetracaine hydrochloride	15K04-B03_322151	1
Fagron	Tetracaine hydrochloride	17G03-B07-345008	2
Orgamol Pharma	Tetracaine hydrochloride	6093547	1
Euro OTC	Tetracaine hydrochloride	1411019	1
Euro OTC	Tetracaine hydrochloride	140502601	1
Euro OTC	Tetracaine hydrochloride	13509155	1

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Supplier	Substance	Batch	Spectra
Fagron	Tetracaine hydrochloride	16G28-B03-332099	2
Phoenix	Tetracaine hydrochloride	15437104	2
Phoenix	Tetracaine hydrochloride	3058	1
Phoenix	Tetracaine hydrochloride	1803001-01	1
Fagron	Tetracaine hydrochloride	14G14-B08-300198	6
Phoenix 04.11.16 Phoeni...	Tetracaine hydrochloride	1607031-01	1
Phoenix am 30.04.2014	Tetracaine hydrochloride	1310006-01	1
Phoenix Goettin	Tetracaine hydrochloride	1409026-01	1
Phönix	Tetracaine hydrochloride	130301201	1
Phönix	Tetracaine hydrochloride	2015E-02039	1
Phönix	Tetracaine hydrochloride	1405026-01	1
Phönix	Tetracaine hydrochloride	1612005-01	1
PHÖNIX	Tetracaine hydrochloride	15437109	1
Sanacorp	Tetracaine hydrochloride	1207001-02	1
Sanacorp	Tetracaine hydrochloride	1303012-01	1
Sanacorp	Tetracaine hydrochloride	15/AKD1	1
Sanacorp	Tetracaine hydrochloride	1409026-01	1
Sanacorp	Tetracaine hydrochloride	17G03-B07-341853	1
Sanacorp, 21.02.17, 13,...	Tetracaine hydrochloride	1607031-01	1
Caelo	Tetracaine hydrochloride	1110010-01	1
Fagron	Tetracaine hydrochloride	1411019-01	1
Caelo	Tetracaine hydrochloride	17G03-B07	1
Sino Phyto	Tetracaine hydrochloride	12019816	1
Synopharm/Anzag	Tetracaine hydrochloride	2712Q-02039	1
VDI 26.09.14 12,00 euro	Tetracaine hydrochloride	1405026-01	1
Fagron	Tetracaine hydrochloride	16G28-B03-327368	13
Caelo	Tetracaine hydrochloride	12019822	6
Caelo	Tetracaine hydrochloride	15437108	1
Euro OTC	Tetracaine hydrochloride		1
Fagron	Tetracaine hydrochloride	15K04-B03-322151	11
Fagron	Tetracaine hydrochloride		1

- 110 244 spectra from 742 *Apo-Ident* customers from a total of 31 660 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tetracaine hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tetracaine hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	345	0	110 344
Type B	0	440	0	118 702
Type C	0	998	5	110 244

The substance/substance group *Tetracaine hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2609 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.6364 %)
Type C	100.0000 % (> 99.8899 %)	99.5015 % (> 99.2024 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tetracaine hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fluocinoloneacetonid, micronized	66.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tetracaine hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22912	22912	0.00	66.72
23162	22912	3.24	67.01
20924	21845	3.68	66.72
21845	21845	0.00	72.59
22285	22285	0.00	73.54
23163	21845	4.00	67.66
23500	21845	6.50	66.59
24141	24141	0.00	79.62

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tetracycline hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20044-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tetracycline hydrochloride; Tetracyclini hydrochloridum

Special notes

When selecting the *Tetracycline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tetracycline hydrochloride	5	6	123

Second-stage model

For differentiation of the substance/substance group *Tetracycline hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tetracycline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tetracycline hyd...	13201303	21427	60	20130807
Caelo	Tetracycline hyd...	13201303	21428	60	20130807
Caelo	Tetracycline hyd...	161167	22468	60	20160504*
Caelo	Tetracycline hyd...	15230712	22833	40	20150819
Euro OTC	Tetracycline hyd...	1302012-01	21079	40	1411585
Euro OTC	Tetracycline hyd...	1506012	21835	60	20150707*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Tetracycline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 369 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 230 spectra of 6 reference samples from the substance/substance group *Tetracycline hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tetracycline hydrochloride	172858	23847	40
Caelo	Tetracycline hydrochloride	181986	24256	40
Caelo	Tetracycline hydrochloride	183083	24394	40
Euro OTC	Tetracycline hydrochloride	1603026	22545	40
Euro OTC	Tetracycline hydrochloride	1706020	23691	30
Euro OTC	Tetracycline hydrochloride	1811031	24450	40

- 118912 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 441 spectra from 225 *Apo-Ident* customers from 126 batches from the substance/substance group *Tetracycline hydrochloride*.
- Among them are spectra of independent samples from 122 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Aliance am 10.03.2014	Tetracycline hydrochloride	1302012-02	1
Alliance Health 22.08.2...	Tetracycline hydrochloride	13201307	1
Bombastus	Tetracycline hydrochloride	1204039-02	1
Bombastus	Tetracycline hydrochloride	1603026-01	2
Bombastus	Tetracycline hydrochloride	1811031-01	1
Caelo	Tetracycline hydrochloride	12353613	1
Caelo	Tetracycline hydrochloride	5091202	1
Caelo	Tetracycline hydrochloride	9248704	1
Caelo	Tetracycline hydrochloride	12138104	1
Caelo	Tetracycline hydrochloride	1302012-01	1
Caelo	Tetracycline hydrochloride	13L10B02296956	1
Caelo	Tetracycline hydrochloride	14364604	3
Caelo	Tetracycline hydrochloride	8682	1
Caelo	Tetracycline hydrochloride	15230703	3
Caelo	Tetracycline hydrochloride	15230714	1
Caelo	Tetracycline hydrochloride	1603026-01	3
Caelo	Tetracycline hydrochloride	15230717	3
Caelo	Tetracycline hydrochloride	2883	1
Caelo	Tetracycline hydrochloride	15230715	3
Caelo	Tetracycline hydrochloride	16116701	3
Caelo	Tetracycline hydrochloride	16116706	4
Caelo	Tetracycline hydrochloride	1017A-02378	1
Caelo	Tetracycline hydrochloride	14364601	1
Caelo	Tetracycline hydrochloride	16116704	1
Caelo	Tetracycline hydrochloride	16116720	1
Caelo	Tetracycline hydrochloride	16116721	5
Caelo	Tetracycline hydrochloride	17285803	7

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Supplier	Substance	Batch	Spectra
Caelo	Tetracycline hydrochloride	1611617	1
Caelo	Tetracycline hydrochloride	17285808	5
Caelo	Tetracycline hydrochloride	18308303	1
Caelo	Tetracycline hydrochloride	18308313	1
Caelo	Tetracycline hydrochloride	13201301	3
Caelo	Tetracycline hydrochloride	14364616	2
Caelo	Tetracycline hydrochloride	16116709	4
Caelo	Tetracycline hydrochloride	1402030-01	1
Caelo	Tetracycline hydrochloride	18198603	1
Caelo	Tetracycline hydrochloride	12353603	6
Caelo	Tetracycline hydrochloride	15230720	3
Caelo	Tetracycline hydrochloride	151018-61	1
Caelo	Tetracycline hydrochloride	13F17-N03	1
Caelo	Tetracycline hydrochloride	1506012-01	2
Caelo	Tetracycline hydrochloride	18308305	1
Caelo	Tetracycline hydrochloride	3314	1
Caelo	Tetracycline hydrochloride	3341	1
Caelo	Tetracycline hydrochloride	1204039	2
Caelo	Tetracycline hydrochloride	4012Q-02378	1
Caelo	Tetracycline hydrochloride	2714U-02378	1
Caelo	Tetracycline hydrochloride	15230707	2
Caelo	Tetracycline hydrochloride	4315I-02378	1
Caelo	Tetracycline hydrochloride	111002901	1
Caelo	Tetracycline hydrochloride	16116715	6
Caelo	Tetracycline hydrochloride	12138106	2
Caelo	Tetracycline hydrochloride	15230711	1
Caelo	Tetracycline hydrochloride	172855809	1
Caelo	Tetracycline hydrochloride	18198602	4
Caelo	Tetracycline hydrochloride	18308302	1
Caelo	Tetracycline hydrochloride	17285801	8
Caelo	Tetracycline hydrochloride	13201309	1
Caelo	Tetracycline hydrochloride	1412007-01	2
Caelo	Tetracycline hydrochloride	14080606	3
Caelo	Tetracycline hydrochloride	166116709	1
Caelo	Tetracycline hydrochloride	1706020-01	1
Caelo	Tetracycline hydrochloride	14H06-B05-313591	1
Caelo	Tetracycline hydrochloride	14364614	1
Caelo	Tetracycline hydrochloride	12353602	1
Caelo	Tetracycline hydrochloride	12353609	1
Caelo	Tetracycline hydrochloride	12353612	1
Caelo	Tetracycline hydrochloride	103201301	1
Caelo	Tetracycline hydrochloride	13201302	1
Caelo	Tetracycline hydrochloride	13201307	1
Caelo	Tetracycline hydrochloride	14080605	2
Caelo	Tetracycline hydrochloride	16116714	1
Caelo	Tetracycline hydrochloride	17285809	5
Caelo	Tetracycline hydrochloride	18198608	6
Caelo	Tetracycline hydrochloride	1811031/01	1
Caesar & Loretz GmbH	Tetracycline hydrochloride	18198612	2
Caesar & Loretz GmbH	Tetracycline hydrochloride	18308305	1
Caesar & Loretz GmbH	Tetracycline hydrochloride	18308313	1
Caesar & Loretz GmbH /E	Tetracycline hydrochloride	18308305	1
Celo/Kehr	Tetracycline hydrochloride	13201307	1
EuRho	Tetracycline hydrochloride	1302012-02	1
EuRho	Tetracycline hydrochloride	1402030-02	1
Eurho/Phoenix	Tetracycline hydrochloride	1204039-02	1
Euro OTC	Tetracycline hydrochloride	1506012-01	27
Euro OTC	Tetracycline hydrochloride	141200701	1
Euro OTC	Tetracycline hydrochloride	1110029-01	2
Euro OTC	Tetracycline hydrochloride	100518-62	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Tetracycline hydrochloride	28021315	1
Euro OTC	Tetracycline hydrochloride	21111404	1
Euro OTC	Tetracycline hydrochloride	150601201	2
Euro OTC	Tetracycline hydrochloride	160621TCH	1
Euro OTC	Tetracycline hydrochloride	21031702	1
Euro OTC	Tetracycline hydrochloride	27101708	1
Euro OTC	Tetracycline hydrochloride	1506012-02Eur	1
Euro OTC	Tetracycline hydrochloride	1706020-01	38
Euro OTC	Tetracycline hydrochloride	1412007-03	7
Euro OTC	Tetracycline hydrochloride	1811031-01	12
Euro OTC	Tetracycline hydrochloride	1204039-01	5
Euro OTC	Tetracycline hydrochloride	140203001	1
Euro OTC	Tetracycline hydrochloride	13042015C	1
Euro OTC	Tetracycline hydrochloride	140410-62	1
Euro OTC	Tetracycline hydrochloride	1603026	2
Euro OTC	Tetracycline hydrochloride	160302601	1
Euro OTC	Tetracycline hydrochloride	1103003-01	1
Euro OTC	Tetracycline hydrochloride	160302	1
Euro OTC	Tetracycline hydrochloride	1204039-02	11
Euro OTC	Tetracycline hydrochloride	1603026-01	33
Euro OTC	Tetracycline hydrochloride	22(1706020-01)	1
Euro OTC	Tetracycline hydrochloride	180306T/1412007-03	1
Euro OTC	Tetracycline hydrochloride	120403902	1
Euro OTC	Tetracycline hydrochloride	1412007-01	9
Euro OTC	Tetracycline hydrochloride	14120007-01	1
Euro OTC	Tetracycline hydrochloride	170602001	1
Euro OTC	Tetracycline hydrochloride	1603026_01	1
Euro OTC	Tetracycline hydrochloride	411682	1
Euro OTC	Tetracycline hydrochloride	12040390	1
Euro OTC	Tetracycline hydrochloride	1706020-02	1
Euro OTG/ AHD	Tetracycline hydrochloride	1706020-01	1
EUro/AHD	Tetracycline hydrochloride	1302012-01	1
Euro/Anzag	Tetracycline hydrochloride	1603026-01	1
euro/phönix	Tetracycline hydrochloride	1506012-01	2
Euro OTC	Tetracycline hydrochloride	1402030-02	7
Euro OTC	Tetracycline hydrochloride	17060201-01	1
Euro OTC	Tetracycline hydrochloride	1706020	2
Euro OTC	Tetracycline hydrochloride	1302012-02	15
Europharm/Otto	Tetracycline hydrochloride	1204039-01	1
Europharm/Otto	Tetracycline hydrochloride	1204039-02	3
Fagron	Tetracycline hydrochloride	12E10-N05	1
Fagron	Tetracycline hydrochloride	13F17-N03	4
Fagron	Tetracycline hydrochloride	14H06-B05-299498	1
Fagron	Tetracycline hydrochloride	14H06-B05-303911	1
Fagron	Tetracycline hydrochloride	14H06-B05	1
Fagron	Tetracycline hydrochloride	14H06-B05-314870	1
Fagron	Tetracycline hydrochloride	12J15-N05	1
Fagron	Tetracycline hydrochloride	1506012-01	1
Fagron	Tetracycline hydrochloride	14H06-B05-303912	6
Fagron	Tetracycline hydrochloride	13L10-B02-294455	2
Fagron	Tetracycline hydrochloride	13J22-N04	1
Fagron	Tetracycline hydrochloride	13L10-B02-294454	1
Fagron	Tetracycline hydrochloride	1402030-02	2
Fagron	Tetracycline hydrochloride	14H06-B05-303912	1
Fagron	Tetracycline hydrochloride	14H06-B05-311707	1
Fagron	Tetracycline hydrochloride	13201301	1
Fagron	Tetracycline hydrochloride	18308305	1
Gatt-Koller	Tetracycline hydrochloride	1700729	1
Gehe	Tetracycline hydrochloride	1110029-01	1
Gehe	Tetracycline hydrochloride	15230703	1

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Supplier	Substance	Batch	Spectra
Gehe	Tetracycline hydrochloride	16116706	1
GEHE	Tetracycline hydrochloride	18198612	1
Caelo	Tetracycline hydrochloride	1160117	1
Euro OTC	Tetracycline hydrochloride	1506012-02	2
Caelo	Tetracycline hydrochloride	14364612	3
Hoff/ Noweda	Tetracycline hydrochloride	14364604	1
Ichthyl/Phönix	Tetracycline hydrochloride	1603026-01	1
Ichthyl-Gesellschaft	Tetracycline hydrochloride	1603026-01	1
Jenne	Tetracycline hydrochloride	1506012-02	1
Jenne	Tetracycline hydrochloride	18198602	1
ningxia	Tetracycline hydrochloride	1412007-01	1
Ningxia	Tetracycline hydrochloride	1603026-01	3
Noweda	Tetracycline hydrochloride	13201307	1
Noweda	Tetracycline hydrochloride	1412007-03	1
Noweda	Tetracycline hydrochloride	18198603	1
Euro OTC	Tetracycline hydrochloride	1402030-01	8
Phoenix	Tetracycline hydrochloride	170602001	3
Phoenix	Tetracycline hydrochloride	18198612	1
Phoenix	Tetracycline hydrochloride	3428	1
PHÖNIX	Tetracycline hydrochloride	16116721	1
Phönix Gotha	Tetracycline hydrochloride	1302012-01	1
Sanacorp	Tetracycline hydrochloride	100403401	1
Sanacorp	Tetracycline hydrochloride	1402030-01	1
Euro OTC	Tetracycline hydrochloride	1302012-01	7
Anzag/euRho	Tetracycline hydrochloride		1
EuRho/AHD	Tetracycline hydrochloride		1
s. Protokoll	Tetracycline hydrochloride		1

- 110 806 spectra from 742 *Apo-Ident* customers from a total of 31 767 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tetracycline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tetracycline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	230	0	118 912
Type C	0	428	13	110 806

The substance/substance group *Tetracycline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.3913 %)
Type C	100.0000 % (> 99.8899 %)	97.0522 % (> 96.3719 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tetracycline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxytetracycline hydrochloride	20.66	—
Chlortetracycline hydrochloride	21.28	—
Eosin Y	26.19	—
Levothyroxin sodium	39.07	—
Sodium cromoglicate	45.69	—
Sulfogaiacol hydrate	55.96	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tetracycline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21428	21835	2.33	32.33
21835	21835	0.00	32.15
22468	22468	0.00	26.19
21079	21079	0.00	27.11
21427	21835	5.37	31.12
22833	21079	7.76	28.52

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Thalidomide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21552-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Thalidomide; Thalidomidum

Special notes

When selecting the *Thalidomide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Thalidomide	5	2	3

Second-stage model

For differentiation of the substance/substance group *Thalidomide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Thalidomide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Thalidomide	13395704	21739	60	20140207
Caelo	Thalidomide	15276711	22880	40	1704508
Caelo	Thalidomide	182496	24399	40	20181022*
Fagron	Thalidomide	14E27B04295348	21552	60	1503608
Fagron	Thalidomide	15A13-B01-312230	22882	40	1704509

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Thalidomide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 449 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Thalidomide*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Thalidomide	162703	22774	40
Caelo	Thalidomide	172100	23684	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Thalidomide*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Thalidomide	20081504	1
Fagron	Thalidomide	14E27-B04-299297	1
Fagron	Thalidomide	13K20-N01	1

- 111 244 spectra from 742 *Apo-Ident* customers from a total of 31 888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Thalidomide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thalidomide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	3	0	111 244

The substance/substance group *Thalidomide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Thalidomide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Indometacin	27.18	—
Dequalinium chloride	36.66	—
Sodium cromoglicate	45.81	—
Ciprofloxacin hydrochloride	47.21	—
Midazolam hydrochloride	47.48	—
Caffeine	53.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thalidomide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22880	22880	0.00	45.34
22882	22882	0.00	77.27
21552	21552	0.00	26.98
21739	24399	13.39	32.38
24399	24399	0.00	43.60

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Theophylline**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20723-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Theophylline; Theophyllinum

Special notes

When selecting the *Theophylline* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Theophylline	3	2	9

Second-stage model

For differentiation of the substance/substance group *Theophylline* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Theophylline*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Theophylline	12166316	20723	40	1402055
Caelo	Theophylline	12341101	21740	60	20121115
Caelo	Theophylline	192563	24902	40	20191120*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Theophylline*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Theophylline*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Theophylline	15203018	23253	40
Caelo	Theophylline	171962	23854	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 16 spectra from 14 *Apo-Ident* customers from 10 batches from the substance/substance group *Theophylline*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Theophylline	12166305	2
Caelo	Theophylline	12166312	3
Caelo	Theophylline	12166315	1
Caelo	Theophylline	12166311	1
Caelo	Theophylline	15203010	1
Caelo	Theophylline	17196203	1
Caelo	Theophylline	12166306	1
Caelo	Theophylline	12341104	1
Caesar&lorenz,Phoenix	Theophylline	12166315	1
Caeser und Loretz GmbH	Theophylline	18097508	1
Noweda	Theophylline	12166305	1
Caelo	Theophylline	12341101	2

- 111 231 spectra from 742 *Apo-Ident* customers from a total of 31 881 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Theophylline* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Theophylline* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	15	1	111 231

The substance/substance group *Theophylline* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Theophylline* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-phenylalanine	52.75	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Theophylline* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20723	20723	0.00	52.75
21740	20723	9.99	55.35
24902	24902	0.00	54.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Theophylline-ethylenediamine hydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20831-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Theophylline-ethylenediamine hydrate; Theophyllinum et ethylenediaminum hydricum

Special notes

When selecting the *Theophylline-ethylenediamine hydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Theophylline-ethylenediamine hydrate	6	2	1

Second-stage model

For differentiation of the substance/substance group *Theophylline-ethylenediamine hydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Theophylline-ethylenediamine hydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Theophylline-eth...	12145301	20831	40	20120628
Caelo	Theophylline-eth...	12363708	20992	40	20130116
Caelo	Theophylline-eth...	13268609	21549	40	1412133
Caelo	Theophylline-eth...	15380302	22589	40	20160211
Caelo	Theophylline-eth...	17073707	23564	30	20170323
Caelo	Theophylline-eth...	192220	24903	40	20191204*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 230 spectra of 6 reference samples from the substance/substance group *Theophylline-ethylenediamine hydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 459 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Theophylline-ethylenediamine hydrate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Theophylline-ethylenediamine...	172999	23823	40
Caelo	Theophylline-ethylenediamine...	182738	24383	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2 spectra from 2 *Apo-Ident* customers from 2 batches from the substance/substance group *Theophylline-ethylenediamine hydrate*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM / Phoenix	Theophylline-ethylenediamine...	KNC0896J14	1
Caelo	Theophylline-ethylenediamine...	15380302	1

- 111 245 spectra from 742 *Apo-Ident* customers from a total of 31 889 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Theophylline-ethylenediamine hydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Theophylline-ethylenediamine hydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	230	0	110 459
Type B	0	80	0	119 062
Type C	0	2	0	111 245

The substance/substance group *Theophylline-ethylenediamine hydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.3913 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8905 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Theophylline-ethylenediamine hydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Miconazole nitrate	44.17	–
Tyrosine	49.68	–
Glycine	53.37	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Theophylline-ethylenediamine hydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20831	21549	4.49	66.17
20992	21549	1.99	64.52
21549	21549	0.00	62.99
22589	24903	3.70	65.73
23564	24903	4.26	59.69
24903	24903	0.00	61.49

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Thiamine chloride hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20566-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Thiamine chloride hydrochloride; Thiamini hydrochloridum

Special notes

When selecting the *Thiamine chloride hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Thiamine chloride hydrochloride	5	4	27

Second-stage model

For differentiation of the substance/substance group *Thiamine chloride hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Thiamine chloride hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Thiamine chlorid...	14069502	21478	60	20140321
Caelo	Thiamine chlorid...	14069502	21511	60	8986
Caelo	Thiamine chlorid...	160156	22477	60	20160316*
Caelo	Thiamine chlorid...	192567	25095	40	20191216*
Euro OTC	Thiamine chlorid...	1211008-02	21647	60	20121122
Euro OTC	Thiamine chlorid...	1612004	22919	40	20170117*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 320 spectra of 6 reference samples from the substance/substance group *Thiamine chloride hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 369 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 160 spectra of 4 reference samples from the substance/substance group *Thiamine chloride hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 4 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Thiamine chloride hydrochlor...	170976	23368	40
Euro OTC	Thiamine chloride hydrochlor...	1705034	23439	40
Euro OTC	Thiamine chloride hydrochlor...	1712013	23911	40
Euro OTC	Thiamine chloride hydrochlor...	1807001	24146	40

- 118982 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 38 spectra from 17 *Apo-Ident* customers from 29 batches from the substance/substance group *Thiamine chloride hydrochloride*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Thiamine chloride hydrochlor...	11371313	1
Caelo	Thiamine chloride hydrochlor...	11061401	1
Caelo	Thiamine chloride hydrochlor...	4071402	1
Caelo	Thiamine chloride hydrochlor...	12091407	1
Caelo	Thiamine chloride hydrochlor...	8121405	1
Caelo	Thiamine chloride hydrochlor...	15199009	2
Caelo	Thiamine chloride hydrochlor...	15199099	1
Caelo	Thiamine chloride hydrochlor...	16015607	1
Caelo	Thiamine chloride hydrochlor...	171201301	1
Caelo	Thiamine chloride hydrochlor...	15269613	1
Caelo	Thiamine chloride hydrochlor...	12340712	1
Caelo	Thiamine chloride hydrochlor...	5122	1
Caelo	Thiamine chloride hydrochlor...	15003201	1
Caelo	Thiamine chloride hydrochlor...	16015609	1
Euro OTC	Thiamine chloride hydrochlor...	161200401	1
Euro OTC	Thiamine chloride hydrochlor...	1705034-01	2
Euro OTC	Thiamine chloride hydrochlor...	1712013-01	1
Euro OTC	Thiamine chloride hydrochlor...	1807001-01	1
Euro OTC	Thiamine chloride hydrochlor...	1211008-01	1
Fagron	Thiamine chloride hydrochlor...	13E22-No8	1
Fagron	Thiamine chloride hydrochlor...	10111401	1
Fagron	Thiamine chloride hydrochlor...	190115006	1
Fagron	Thiamine chloride hydrochlor...	17F23-B02-340810	1
Finze	Thiamine chloride hydrochlor...	9216114	1
Caelo	Thiamine chloride hydrochlor...	11371319	3
Caelo	Thiamine chloride hydrochlor...	13296610	4
Sanacorp	Thiamine chloride hydrochlor...	12340712	1
Caelo	Thiamine chloride hydrochlor...	11371309	2
Caelo	Thiamine chloride hydrochlor...		1
Caelo	Thiamine chloride hydrochlor...	14069502	1

- 111 209 spectra from 742 *Apo-Ident* customers from a total of 31 863 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Thiamine chloride hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thiamine chloride hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	320	0	110 369
Type B	0	160	0	118 982
Type C	0	38	0	111 209

The substance/substance group *Thiamine chloride hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 84.2105 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Thiamine chloride hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium citrate	40.00	—
Menthol	45.48	—
Estradiol hemihydrate	52.22	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thiamine chloride hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22477	22477	0.00	40.98
21478	21511	7.37	43.35
21511	21511	0.00	43.47
21647	22477	5.56	41.04
22919	22919	0.00	42.61
25095	25095	0.00	43.74

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Thymol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20003-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Thymol; Thymolum

Special notes

When selecting the *Thymol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Thymol	5	5	55

Second-stage model

For differentiation of the substance/substance group *Thymol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Thymol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Thymol	14025805	21469	60	20140127
Caelo	Thymol	16144101	23160	40	20160606
Euro OTC	Thymol	1312022-02	21639	60	20131219
Euro OTC	Thymol	1510004	21943	60	20151016*
Fagron	Thymol	15H13-B05-328912	23499	40	20151118

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 260 spectra of 5 reference samples from the substance/substance group *Thymol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 429 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Thymol*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Thymol	173407	23837	40
Caelo	Thymol	181424	24231	40
Caelo	Thymol	190342	24552	40
Euro OTC	Thymol	1710037	23773	40
Euro OTC	Thymol	1808014	24299	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 116 spectra from 90 *Apo-Ident* customers from 57 batches from the substance/substance group *Thymol*.
- Among them are spectra of independent samples from 55 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM / Herba	Thymol	KNC1166J14	1
Caelo	Thymol	13288802	4
Caelo	Thymol	11358616	1
Caelo	Thymol	19061303	1
Caelo	Thymol	13147502	2
Caelo	Thymol	13288806	1
Caelo	Thymol	14025809	2
Caelo	Thymol	14025807	1
Caelo	Thymol	2031503	1
Caelo	Thymol	14025816	1
Caelo	Thymol	14310601	1
Caelo	Thymol	14310605	1
Caelo	Thymol	15362901	5
Caelo	Thymol	16144105	7
Caelo	Thymol	161441108	1
Caelo	Thymol	17324203	2
Caelo	Thymol	14025802	2
Caelo	Thymol	21042	1
Caelo	Thymol	11178718	1
Caelo	Thymol	14025815	1
Caelo	Thymol	15362908	3
Caelo	Thymol	1730711	1
Caelo	Thymol	14302401	1
Caelo	Thymol	17340711	3
Caelo	Thymol	15130101	2
Caesar & Loretz GmbH	Thymol	16144101	1
Caesar & Loretz GmbH	Thymol	17340716	1
Caesar & Loretz GmbH/No...	Thymol	18221907	1
Caesar § Lorenz GmbH	Thymol	13288806	1
Ebert & Jacobi 02.08...	Thymol	15362901	1
Euro OTC	Thymol	20151012-1	1
Euro OTC	Thymol	11358603	1
Euro OTC	Thymol	1510004-03	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Thymol	1710037-01	3
Euro OTC	Thymol	1808014-01	2
Euro/ Phönix	Thymol	1510004-02	1
Euro/Phönix	Thymol	180801401	1
Euro OTC	Thymol	1202028-01	1
Euro OTC	Thymol	1312022-01	1
Euro OTC	Thymol	1510004-02	8
Euro OTC	Thymol	1410007-01	5
Euro OTC	Thymol	1510004-01	2
Fagron	Thymol	713575	1
Fagron	Thymol	12K01-N02	2
Fagron	Thymol	12B06-N11	1
Fagron	Thymol	12H29-N02	2
Fagron	Thymol	12E30-N11	1
Frey+Lau GmbH/Phönix	Thymol	1312022-01	1
Caelo	Thymol	16144108	3
Gehe Kassel	Thymol	1312022-01	1
Caelo	Thymol	11358607	2
Fagron	Thymol	12M29-N02	1
L12	Thymol	15172002	1
L30	Thymol	1510004-03	1
Euro OTC	Thymol	15100004-03	1
Noweda	Thymol	12k01-no2	1
Noweda	Thymol	16144105	1
Phoenix	Thymol	19034205	1
PHOENIX 26.03.2014	Thymol	14025802	2
Phönix	Thymol	11358610	1
Phönix	Thymol	1510004-01	1
Caelo	Thymol	15130106	3
Sanacorp	Thymol	1135816	1
Sanacorp	Thymol	9E14-N16	1
Caelo	Thymol	11358608	1
Caelo	Thymol	16144101	4
Caelo	Thymol	14025805	1
	Thymol	14025802	1

- 111 131 spectra from 742 *Apo-Ident* customers from a total of 31 834 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Thymol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thymol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	260	0	110 429
Type B	0	200	0	118 942
Type C	0	116	0	111 131

The substance/substance group *Thymol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.6923 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 94.8276 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Thymol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Metronidazole	40.20	–
Choline hydrogen tartrate	70.25	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thymol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21469	21943	13.04	70.44
21639	21943	18.70	70.43
21943	21943	0.00	65.15
23160	21943	21.62	70.84
23499	21943	11.65	69.95

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical

variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tobramycin sulfate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20951-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tobramycin sulfate; Tobramycin sulphate; Tobramycini sulfas

Special notes

When selecting the *Tobramycin sulfate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tobramycin sulfate	10	2	9

Second-stage model

For differentiation of the substance/substance group *Tobramycin sulfate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tobramycin sulfate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Tobramycin sulfate	AP15061047002T	22393	40	1608462
Audor Pharma	Tobramycin sulfate	AP15061047002T	23502	40	20160322
Euro OTC	Tobramycin sulfate	1301011-02	21624	60	1508071
Euro OTC	Tobramycin sulfate	1505015-01	21832	60	8963
Euro OTC	Tobramycin sulfate	1510035-01	22240	60	9202
Euro OTC	Tobramycin sulfate	1510035	22252	60	20151208*
Euro OTC	Tobramycin sulfate	1807045	24321	40	20180917*
Euro OTC	Tobramycin sulfate	2001010	25100	40	20200113*
Fagron	Tobramycin sulfate	12G03-N03	20951	40	1404541
Fagron	Tobramycin sulfate	15I17-B04-315697	22359	45	20150928
Fagron	Tobramycin sulfate	16B05-B03-336397	23515	40	1801385

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 525 spectra of 11 reference samples from the substance/substance group *Tobramycin sulfate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 164 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 260 spectra of 5 reference samples from the substance/substance group *Tobramycin sulfate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Tobramycin sulfate	1710029	23870	40
Euro OTC	Tobramycin sulfate	1910008	25085	40
Euro OTC	Tobramycin sulfate	1505015-01	21832SI [†]	60
Euro OTC	Tobramycin sulfate	1510035-01	22240SI [†]	60
Euro OTC	Tobramycin sulfate	1510035	22252SI [†]	60

- 118 882 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 18 spectra from 7 *Apo-Ident* customers from 12 batches from the substance/substance group *Tobramycin sulfate*.
- Among them are spectra of independent samples from 9 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Tobramycin sulfate	16B05-B03-317988	2
Euro OCT/Noweda	Tobramycin sulfate	1510035-01	1
Euro OTC	Tobramycin sulfate	15I17-B04-315697	1
Fagron	Tobramycin sulfate	15/17-B04-315697	1
Fagron	Tobramycin sulfate	16B05-B03	4
Fagron	Tobramycin sulfate	16B05-B03-319433	1
Fagron	Tobramycin sulfate	16B05-B03-330974	2
Fagron	Tobramycin sulfate	17E05-B03-338122	2
Fagron	Tobramycin sulfate	13H09-N09	1
Fagron	Tobramycin sulfate	17J12-B04-341324	1
PHOENIX 31.01.2014	Tobramycin sulfate	1202006-01	1
Euro OTC	Tobramycin sulfate	1505015-01	1

- 111 229 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Validation results

The validation runs checked whether the substance/substance group *Tobramycin sulfate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tobramycin sulfate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	525	0	110 164
Type B	0	203	57	118 882
Type C	0	15	3	111 229

The substance/substance group *Tobramycin sulfate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.8571 %)
Type B	100.0000 % (> 99.9893 %)	78.0769 % (> 76.9231 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tobramycin sulfate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Zinc gluconate	16.62	—
Trometamol	24.63	—
Aciclovir	34.74	—
Calcium lactate pentahydrate	36.17	—
Magnesium citrate	38.27	—
Arginine	39.40	—
Carmellose sodium (400 / 450 / 500 / 6...	41.98	—
Calcium glycerophosphate	42.95	—
Neomycin sulfate	44.06	—
Uridine	46.48	—
Levothyroxin sodium	47.46	—
Tartaric acid	48.52	—
Menthol	50.58	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tobramycin sulfate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22359	21832	8.66	21.67
23515	23515	0.00	21.50
25100	25100	0.00	23.12
24321	24321	0.00	29.22
23502	25100	7.08	24.90
20951	20951	0.00	17.65
22252	22252	0.00	18.23
22393	22393	0.00	18.40
21624	21624	0.00	19.67
21832	21832	0.00	18.72
22240	22240	0.00	31.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group	Tosylchloramide sodium
Substance class	APIs & excipients, solid
Report date	14/07/2020
Report number	20133-2020-07-14
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Tosylchloramide sodium; Tosylchloramidum natricum

Special notes

When selecting the *Tosylchloramide sodium* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tosylchloramide sodium	4	2	33

Second-stage model

For differentiation of the substance/substance group *Tosylchloramide sodium* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tosylchloramide sodium*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tosylchloramide ...	13103201	20864	40	20130424
Caelo	Tosylchloramide ...	13361602	21115	40	1407634
Caelo	Tosylchloramide ...	16236603	23562	40	20160819
Caelo	Tosylchloramide ...	172265	24238	40	20170906*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 4 reference samples from the substance/substance group *Tosylchloramide sodium*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 529 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Tosylchloramide sodium*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tosylchloramide sodium	13361606	21480	60
Caelo	Tosylchloramide sodium	162366	22773	40

- 119042 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 80 spectra from 48 *Apo-Ident* customers from 34 batches from the substance/substance group *Tosylchloramide sodium*.
- Among them are spectra of independent samples from 33 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag	Tosylchloramide sodium	12H09-N01	1
Caelo	Tosylchloramide sodium	11116708	1
Caelo	Tosylchloramide sodium	12323605	1
Caelo	Tosylchloramide sodium	12323606	1
Caelo	Tosylchloramide sodium	12323607	1
Caelo	Tosylchloramide sodium	13103210	2
Caelo	Tosylchloramide sodium	13103206	8
Caelo	Tosylchloramide sodium	1310206	1
Caelo	Tosylchloramide sodium	13361606	3
Caelo	Tosylchloramide sodium	13361607	6
Caelo	Tosylchloramide sodium	16236607	6
Caelo	Tosylchloramide sodium	16236611	2
Caelo	Tosylchloramide sodium	15183905	1
Caelo	Tosylchloramide sodium	14183509	1
Caelo	Tosylchloramide sodium	15039603	4
Caelo	Tosylchloramide sodium	12323609	2
Caelo	Tosylchloramide sodium	13103207	1
Caelo	Tosylchloramide sodium	17061503	2
Caelo	Tosylchloramide sodium	15370505	2
Caelo	Tosylchloramide sodium	71051187	2
Caelo	Tosylchloramide sodium	72215377	2
Caelo	Tosylchloramide sodium	17061511	1
Caelo	Tosylchloramide sodium	15370501	5
Caelo	Tosylchloramide sodium	17226503	3
Caeolo	Tosylchloramide sodium	16236607	1
EuRho	Tosylchloramide sodium	133610607	1
Fagron	Tosylchloramide sodium	11L08-N04	1
Fagron	Tosylchloramide sodium	14L12-B01-301915	1
Fagron	Tosylchloramide sodium	14B27-B03-291967	1
Caelo	Tosylchloramide sodium	16236603/1180117	1
Hydra International Ltd	Tosylchloramide sodium	91020132	1
L10	Tosylchloramide sodium	16236607	2
Lysiform	Tosylchloramide sodium	K-09-2019	1
Caelo	Tosylchloramide sodium	12277005	3
Sanacorp	Tosylchloramide sodium	12H09-N01	1
Taoasis	Tosylchloramide sodium	1623607	1
Caelo	Tosylchloramide sodium	16236603	6

- 111 167 spectra from 742 *Apo-Ident* customers from a total of 31 858 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tosylchloramide sodium* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tosylchloramide sodium* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	86	14	119 042
Type C	0	73	7	111 167

The substance/substance group *Tosylchloramide sodium* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	86.0000 % (> 83.0000 %)
Type C	100.0000 % (> 99.8899 %)	91.2500 % (> 87.5000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tosylchloramide sodium* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	27.90	—
Sodium cromoglicate	28.28	—
Oxytetracycline hydrochloride	32.48	—
Chloramphenicol	33.44	—
Melatonin	35.81	—
Eosin Y	42.68	—
Choline hydrogen tartrate	52.57	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/substance group *Tosylchloramide sodium* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20864	21115	9.82	28.45
21115	21115	0.00	30.50
24238	24238	0.00	30.02
23562	21115	11.15	30.83

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tranexamic acid**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20397-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tranexamic acid; Acidum tranexamicum

Special notes

When selecting the *Tranexamic acid* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tranexamic acid	6	1	27

Second-stage model

For differentiation of the substance/substance group *Tranexamic acid* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tranexamic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Tranexamic acid	APX1508016MT	23504	40	20170224
Audor Pharma	Tranexamic acid	APX1803027MT	24708	40	20180430
Euro OTC	Tranexamic acid	2002005	25078	40	20200219*
Euro OTC	Tranexamic acid	2001034	25099	40	20200218*
Fagron	Tranexamic acid	14C21-B08-292225	21654	60	AR-17-FG-016394-01
Fagron	Tranexamic acid	14L15-B06-3000036	21727	60	AR-15-FG-008937-02

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Tranexamic acid*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 90 spectra of 2 reference samples from the substance/substance group *Tranexamic acid*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Tranexamic acid	16E31-B07-331591	23503	50
Fagron	Tranexamic acid	16E31-B07-331591	23505	40

- 119 052 spectra from a total of 2419 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 44 spectra from 32 *Apo-Ident* customers from 29 batches from the substance/substance group *Tranexamic acid*.
- Among them are spectra of independent samples from 27 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Tranexamic acid	APX1712011MT	7
Audor Pharma	Tranexamic acid	1508016MT	1
Audor Pharma	Tranexamic acid	APX1611013MT	3
Audor Pharma	Tranexamic acid	X1611013M	2
Audor Pharma	Tranexamic acid	X1712011M	1
Audor Pharma	Tranexamic acid	X1803027M	1
Audor Pharma	Tranexamic acid	APX17112011MT	1
Caelo	Tranexamic acid	15J29-B04	1
Fagron	Tranexamic acid	16J29-B04-312372	1
Fagron	Tranexamic acid	12D11-N02	1
Fagron	Tranexamic acid	13G24-N21	1
Fagron	Tranexamic acid	16B03-B02-319617	2
Fagron	Tranexamic acid	13D08-N240002/40	1
Fagron	Tranexamic acid	5041804	1
Fagron	Tranexamic acid	18J25-B05-354991	1
Fagron	Tranexamic acid	18J25-B05	1
Fagron	Tranexamic acid	15J29-B04	1
Fagron	Tranexamic acid	13D08-N24	1
Fagron	Tranexamic acid	13D08-N24	1
Fagron	Tranexamic acid	15J29-B04-312372	1
Fagron	Tranexamic acid	18A17-B05-345038	1
Fagron	Tranexamic acid	18F20-B01-351693	1
Fagron	Tranexamic acid	18F20-B01	1
Fagron	Tranexamic acid	13K08-B04-287966	1
Fagron	Tranexamic acid	18F20-B01-351691	3
Noweda	Tranexamic acid	18a17-b05-345037	1
Caelo	Tranexamic acid	18/25-B05-354991	1
Sanacorp	Tranexamic acid	16E31-B07-331591	1
Audor Pharma	Tranexamic acid	APX1508016MT	2
Audor Pharma	Tranexamic acid	APX1803027MT	2

- 111 203 spectra from 742 *Apo-Ident* customers from a total of 31 863 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#),

the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tranexamic acid* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tranexamic acid* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	90	0	119 052
Type C	0	39	5	111 203

The substance/substance group *Tranexamic acid* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 93.3333 %)
Type C	100.0000 % (> 99.8899 %)	88.6364 % (> 81.8182 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tranexamic acid* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Stearic acid 50	50.43	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tranexamic acid* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21654	21654	0.00	70.69
21727	21727	0.00	67.59
23504	25099	1.84	68.70
25078	25078	0.00	69.39
25099	25099	0.00	69.19
24708	25099	2.60	69.36

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tretinoin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20474-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tretinoin; Tretinoinum

Special notes

When selecting the *Tretinoin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tretinoin	6	11	219

Second-stage model

For differentiation of the substance/substance group *Tretinoin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tretinoin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Tretinoin	15028403	21757	60	1507086
Caelo	Tretinoin	15028403	21757SI	60	1507086
Caelo	Tretinoin	15239503	21878	60	20150717
Caelo	Tretinoin	15239503	21878SI	60	20150717
Euro OTC	Tretinoin	1402007-02	21747	60	1507085
Euro OTC	Tretinoin	1402007-02	21747SI	60	1507085
Euro OTC	Tretinoin	1510007	21940	60	20151102*
Euro OTC	Tretinoin	1510007	21940SI	60	20151102*
Euro OTC	Tretinoin	1604059	22574	40	20160603*
Fagron	Tretinoin	15F01-B06-317884	22936	40	20150619
Fagron	Tretinoin	15F01-B06-317884	22936SI	40	20150619

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 600 spectra of 11 reference samples from the substance/substance group *Tretinoin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 089 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 900 spectra of 23 reference samples from the substance/substance group *Tretinoin*.
- Among them are spectra of independent samples from 11 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Tretinoin	162915	22779	40
Caelo	Tretinoin	162171	22780	40
Caelo	Tretinoin	172731	23680	40
Caelo	Tretinoin	173057	23843	40
Caelo	Tretinoin	181673	24251	40
Caelo	Tretinoin	181674	24258	40
Euro OTC	Tretinoin	1612010	22911	40
Euro OTC	Tretinoin	1804005	24061	40
Euro OTC	Tretinoin	1901001	24456	40
Euro OTC	Tretinoin	1907014	24855	40
Fagron	Tretinoin	18J30-B02-358547	24824	40
Caelo	Tretinoin	162915	22779SI	40
Caelo	Tretinoin	162171	22780SI	40
Caelo	Tretinoin	172731	23680SI	40
Caelo	Tretinoin	173057	23843SI	40
Caelo	Tretinoin	181673	24251SI	20
Caelo	Tretinoin	181674	24258SI	40
Euro OTC	Tretinoin	1604059	22574SI [†]	40
Euro OTC	Tretinoin	1612010	22911SI	40
Euro OTC	Tretinoin	1804005	24061SI	40
Euro OTC	Tretinoin	1901001	24456SI	40
Euro OTC	Tretinoin	1907014	24855SI	40
Fagron	Tretinoin	18J30-B02-358547	24824SI	40

- 118 242 spectra from a total of 2408 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 715 spectra from 329 *Apo-Ident* customers from 223 batches from the substance/substance group *Tretinoin*.
- Among them are spectra of independent samples from 218 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Tretinoin	16K03-806328-388	1
AHD	Tretinoin	16070002	1
AHD	Tretinoin	1901001-01	1
Fagron	Tretinoin	1510007-02	1
Euro OTC	Tretinoin	1604059-02	17

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Fagron	Tretinoin	17357007	1
Anzag	Tretinoin	14L24B01303157	1
Anzag	Tretinoin	15078305	1
Anzag/Henry Lamotte	Tretinoin	15078303	1
Apo Ident/ Noweda	Tretinoin	1804005-01	1
BASF	Tretinoin	1402007-03	1
BASF / Phönix	Tretinoin	1604059-02	1
BASF/Phönix	Tretinoin	1304028-02	2
Bombastus	Tretinoin	1402007-03	1
Caelo	Tretinoin	16F14-B04-326181	1
Caelo	Tretinoin	12102902	1
Caelo	Tretinoin	11225506	1
Caelo	Tretinoin	11284703	1
Caelo	Tretinoin	11225504	1
Caelo	Tretinoin	711212563	1
Caelo	Tretinoin	5012I-02563	1
Caelo	Tretinoin	12320201	2
Caelo	Tretinoin	12I06-N01	1
Caelo	Tretinoin	12023309	1
Caelo	Tretinoin	3041302	1
Caelo	Tretinoin	12320205	5
Caelo	Tretinoin	12320301	1
Caelo	Tretinoin	12320204	1
Caelo	Tretinoin	12320203	2
Caelo	Tretinoin	12102903	2
Caelo	Tretinoin	12320209	6
Caelo	Tretinoin	12320303	1
Caelo	Tretinoin	12367101	2
Caelo	Tretinoin	12023303	1
Caelo	Tretinoin	12367104	1
Caelo	Tretinoin	13195003	1
Caelo	Tretinoin	13195008	1
Caelo	Tretinoin	14093502	4
Caelo	Tretinoin	14252801	1
Caelo	Tretinoin	14040507	1
Caelo	Tretinoin	14252702	4
Caelo	Tretinoin	1452802	1
Caelo	Tretinoin	15078303	1
Caelo	Tretinoin	15078308	1
Caelo	Tretinoin	15078305	2
Caelo	Tretinoin	151000701	1
Caelo	Tretinoin	1510007-02	1
Caelo	Tretinoin	15437301	1
Caelo	Tretinoin	15F01-B06-308856	1
Caelo	Tretinoin	15437303	13
Caelo	Tretinoin	16070003	1
Caelo	Tretinoin	16291503	6
Caelo	Tretinoin	16F14-B04-324636	1
Caelo	Tretinoin	160405901	1
Caelo	Tretinoin	1517E-02563	1
Caelo	Tretinoin	17106102	10
Caelo	Tretinoin	16217108	3
Caelo	Tretinoin	17106103	1
Caelo	Tretinoin	171061025343	1
Caelo	Tretinoin	1604059-02	1
Caelo	Tretinoin	172773102	1
Caelo	Tretinoin	17305701	8
Caelo	Tretinoin	17305702	6
Caelo	Tretinoin	12959AX20	1
Caelo	Tretinoin	1723102	1

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Supplier	Substance	Batch	Spectra
Caelo	Tretinoin	17357007	5
Caelo	Tretinoin	17305708	1
Caelo	Tretinoin	1804005-01	5
Caelo	Tretinoin	17305709	1
Caelo	Tretinoin	17357008	3
Caelo	Tretinoin	18167401	5
Caelo	Tretinoin	18167301	1
Caelo	Tretinoin	18167408	1
Caelo	Tretinoin	18167309	11
Caelo	Tretinoin	18167410	1
Caelo	Tretinoin	19050003	3
Caelo	Tretinoin	19257102	2
Caelo	Tretinoin	15H31-B01	1
Caelo	Tretinoin	18167409	1
Caelo	Tretinoin	16217112	1
Caelo	Tretinoin	13278105	2
Caelo	Tretinoin	17357002	3
Caelo	Tretinoin	15239501	2
Caelo	Tretinoin	13278104	2
Caelo	Tretinoin	14252710	2
Caelo	Tretinoin	16070002	2
Caelo	Tretinoin	15078302	2
Caelo	Tretinoin	15078301	1
Caelo	Tretinoin	15078307	3
Caelo	Tretinoin	18167302	2
Caelo	Tretinoin	17357005	2
Caelo	Tretinoin	173057075597	1
Caelo	Tretinoin	16F14-B04	1
Caelo	Tretinoin	12D05-N08	1
Caelo	Tretinoin	12320207	1
Caelo	Tretinoin	18167403	2
Caelo	Tretinoin	14040504	5
Caelo	Tretinoin	1109014-02	1
Caelo	Tretinoin	13195002	14
Caelo	Tretinoin	131950002	1
Caelo	Tretinoin	13308004	4
Caelo	Tretinoin	15239502	5
Caelo	Tretinoin	16291502	5
Caelo	Tretinoin	16217122	1
Caelo	Tretinoin	17357001	8
Caelo	Tretinoin	17357009	2
Caelo	Tretinoin	17305710	2
Caelo	Tretinoin	19050001	2
Caelo	Tretinoin	14L24-B01-303157	2
Caelo	Tretinoin	14252706	2
Caelo	Tretinoin	11225511	1
Caelo	Tretinoin	12023302	9
Caelo	Tretinoin	16217107	1
Caelo	Tretinoin	12367103	2
Caelo	Tretinoin	1411016-01	2
Caelo	Tretinoin	17106101	3
Caelo	Tretinoin	16217120	1
Caelo	Tretinoin	20120601	1
Caelo	Tretinoin	13278102	4
Caelo	Tretinoin	17305711	1
Caelo	Tretinoin	1304028-02	3
Caelo	Tretinoin	1735707	1
Caelo	Tretinoin	18167307	3
Caelo	Tretinoin	14093503	1
Caesar & Loretz GmbH	Tretinoin	11225515	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Tretinoin	12320211	1
Caesar & Loretz GmbH	Tretinoin	18167302	1
Caesar & Loretz GmbH	Tretinoin	18167408	1
Caesar & Loretz GmbH	Tretinoin	18167401	1
Caesar & Loretz GmbH	Tretinoin	19050001	1
Caesar & Loretz GmbH, 4. ...	Tretinoin	12023302	1
Caesar & Loretz GmbH/al. ...	Tretinoin	19185802	1
cealo	Tretinoin	13195002	1
Celo	Tretinoin	15437303	1
Celo/Kehr	Tretinoin	16217122	1
EuRho	Tretinoin	151007-01	1
Euro OTC	Tretinoin	16004059-02	1
EuRho/Sanacorp	Tretinoin	130402802	1
Eurimpharm	Tretinoin	1411016-01	1
Euro	Tretinoin	14111016-01	1
Euro OCT Pharma/Fiebig	Tretinoin	1604059-01	2
Euro OTC	Tretinoin	1402007	1
Euro OTC	Tretinoin	141107602	1
Euro OTC	Tretinoin	151000702	1
Euro OTC	Tretinoin	160405901	1
Euro OTC	Tretinoin	162010-02	1
Euro OTC	Tretinoin	130402802	1
Euro OTC	Tretinoin	140200701	1
Euro OTC	Tretinoin	1604059-01	20
Euro OTC	Tretinoin	12959AX20	2
Euro OTC	Tretinoin	161201001	1
Euro OTC	Tretinoin	180400501	1
Euro OTC	Tretinoin	18167405	1
Euro OTC	Tretinoin	190100101	2
Euro OTC	Tretinoin	190100102	1
Euro OTC	Tretinoin	1907014-01	3
Euro OTC	Tretinoin	1901001-02	3
Euro OTC	Tretinoin	18432003	3
Euro OTC	Tretinoin	190100-01	1
Euro OTC	Tretinoin	1510007-01	12
Euro OTC	Tretinoin	161210-01	1
Euro OTC	Tretinoin	819081-16	1
Euro OTC	Tretinoin	1510007-02	14
Euro OTC	Tretinoin	1008021-02	1
Euro OTC	Tretinoin	10429AX21	1
Euro OTC	Tretinoin	1304028-02	4
Euro OTC	Tretinoin	30042014A	1
Euro OTC	Tretinoin	130102802	1
Euro OTC	Tretinoin	141101602	1
Euro OTC	Tretinoin	151000	1
Euro OTC	Tretinoin	1411016-02	11
Euro OTC	Tretinoin	1109014-02	2
Euro OTC	Tretinoin	140007-02	1
Euro OTC	Tretinoin	13041028-01	1
Euro OTC	Tretinoin	1411016-01	9
Euro OTC	Tretinoin	1804005-01	28
Euro OTC	Tretinoin	1304028-01	7
Euro OTC	Tretinoin	1402007-01	5
Euro OTC	Tretinoin	14020007-01	1
Euro OTC	Tretinoin	1612010-01	24
Euro OTC	Tretinoin	1901001-01	19
Euro/Gehe	Tretinoin	1604059-01	1
Euro/Noweda	Tretinoin	1612010-01	1
Euro/Phoenix	Tretinoin	1907014-01	1
Euro/Phönix	Tretinoin	18J30B02359836	1

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Supplier	Substance	Batch	Spectra
Euro/Sanacorp	Tretinoin	1604059-02	1
Euro OTC	Tretinoin	14101602	1
Euro OTC	Tretinoin	18167302	1
Euro OTC	Tretinoin	165070002	1
Euro OTC	Tretinoin	1402007-03	3
Euro OTC	Tretinoin	12059AX20	2
Euro OTC	Tretinoin	160405902	2
Fagron	Tretinoin	18A10-B03-344364	1
Fagron	Tretinoin	11K29-N01	1
Fagron	Tretinoin	13B05-B02-287360	4
Fagron	Tretinoin	13C11-N06	2
Fagron	Tretinoin	13D30N14	1
Fagron	Tretinoin	14093505	1
Fagron	Tretinoin	14D09-B04-293225	1
Fagron	Tretinoin	14D09-B04-293224	1
Fagron	Tretinoin	14D09-B04-293594	1
Fagron	Tretinoin	1440104	1
Fagron	Tretinoin	1410001594	1
Fagron	Tretinoin	14D09-B04-295551	1
Fagron	Tretinoin	14L24-B01-303152	1
Fagron	Tretinoin	15F01-B06-308722	7
Fagron	Tretinoin	15F01-B06-315491	1
Fagron	Tretinoin	231115T	1
Fagron	Tretinoin	16F14-B04	3
Fagron	Tretinoin	1604059-01	1
Fagron	Tretinoin	16K03-B06-328388	5
Fagron	Tretinoin	16K03-B06	3
Fagron	Tretinoin	17273102	1
Fagron	Tretinoin	17K01-B05-341941	2
Fagron	Tretinoin	17K01-B05-345784	2
Fagron	Tretinoin	17K01-B05-347435	1
Fagron	Tretinoin	17K01-B05-341936	6
Fagron	Tretinoin	16F14B04325560	1
Fagron	Tretinoin	14009-804	1
Fagron	Tretinoin	15F01-B06-308856	2
Fagron	Tretinoin	18J30-B02-358540	2
Fagron	Tretinoin	16F14-B04-324636	1
Fagron	Tretinoin	13B05-B02-287361	2
Fagron	Tretinoin	18j30B02358540	1
Fagron	Tretinoin	18J30-B02-359836	1
Fagron	Tretinoin	16F14B04325560	1
Fagron	Tretinoin	12I06-N01	2
Fagron	Tretinoin	16F14-B04-326181	2
Fagron	Tretinoin	16F14-B04-325567	1
Fagron	Tretinoin	12I06-N01	1
Fagron	Tretinoin	170706TTRER-20151004	1
Fagron	Tretinoin	17K01-B05-347436	1
Fagron	Tretinoin	20120601	1
Fagron	Tretinoin	14040504	1
Fagron	Tretinoin	15F01-B06-313216	2
Fagron	Tretinoin	TRER-20180703	2
Fagron	Tretinoin	13D30-N14-3365319091	1
Fagron	Tretinoin	14L24-B01	1
Fagron	Tretinoin	14L24-B01-303157	3
Fargon	Tretinoin	16K03-B06-328388	1
Fargron	Tretinoin	14D09-B04-293225	1
Fargron	Tretinoin	1402007-01	1
FEJ	Tretinoin	15F01-B06-308856	1
Fiebig	Tretinoin	1612010-01	1
Gatt-Koller	Tretinoin	606210909	1

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Supplier	Substance	Batch	Spectra
Gatt-Koller	Tretinoin	1702180	1
Gatt-Koller	Tretinoin	1804193	1
Gehe	Tretinoin	15437303	1
Gehe	Tretinoin	1612010-01	1
Gehe	Tretinoin	19050001	1
Gehe	Tretinoin	1901001-01	1
Gehe	Tretinoin	1907014-01	1
GEHE	Tretinoin	19050001	1
Fagron	Tretinoin	13D30-N14	2
Gehe am 11.10.2017	Tretinoin	17106102	1
Caelo	Tretinoin	13B05-B02-287360	1
Caelo	Tretinoin	17305707	6
Caelo	Tretinoin	17305704	4
Euro OTC	Tretinoin	1612010-02	12
Euro OTC	Tretinoin	18062082	1
Euro OTC	Tretinoin	17357001	1
Gehe-Eurho 22.11.2017	Tretinoin	2171127Ma7	1
Geibo	Tretinoin	17K01-B05-341936	1
JENNE	Tretinoin	17K01-B05-341941	1
Fagron	Tretinoin	17K01-B05-349946	2
Kehr	Tretinoin	1604059-01	1
Krieger	Tretinoin	1612010-02	2
Krieger am 17.08.2018	Tretinoin	17K01-B05-345784	1
L10	Tretinoin	1612010-01	2
Nachprüfung	Tretinoin	2605001-01	1
Noweda	Tretinoin	12023302	2
Noweda	Tretinoin	13D30-N14	1
Noweda	Tretinoin	15078307	1
Noweda	Tretinoin	15F01-B06-315491	1
Caelo	Tretinoin	13278101	1
Euro OTC	Tretinoin	140200703	1
Phoenix	Tretinoin	12367103	1
Phoenix	Tretinoin	15F01-B06-317884	1
phönix	Tretinoin	1612010-01	1
Phönix	Tretinoin	1109014-02	1
Phönix	Tretinoin	14D09-B04	2
Phönix	Tretinoin	14D09-B04-293224	1
Phönix	Tretinoin	1402007-02	1
Phönix	Tretinoin	3144	1
Phönix WE:04.01.18 E.K. ...	Tretinoin	17273102	1
Caelo	Tretinoin	13308003	1
Fagron	Tretinoin	16F14-B04-325560	2
Caelo	Tretinoin	16070001	1
Fagron	Tretinoin	17K01B05349946	1
Sanacorp	Tretinoin	12320302	1
Sanacorp	Tretinoin	12/06-N01	1
Sanacorp	Tretinoin	13308004	1
Sanacorp	Tretinoin	1411016-01	1
Sanacorp	Tretinoin	1411016-02	1
Sanacorp	Tretinoin	16217122	1
Sanacorp	Tretinoin	17357001	1
Sanacorp	Tretinoin	1804005-01	1
Caelo	Tretinoin	1901001-01	2
Fagron	Tretinoin	17K01-B05	2
Fagron	Tretinoin	1411016-01	1
Caelo	Tretinoin	12102904	2
Caelo	Tretinoin	1612010-01	4
WE:Phönix 20.08.2016 E. ...	Tretinoin	1510007-02	1
WE:Phönix 02.11..2016 ...	Tretinoin	1604059-01	1
Caelo	Tretinoin		1

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Supplier	Substance	Batch	Spectra
Caelo	Tretinoin	15239503	2
Euro OTC	Tretinoin	1402007-02	8
Fagron	Tretinoin	15F01-B06-317884	1
Nachprüfung	Tretinoin		1

- 110 532 spectra from 742 *Apo-Ident* customers from a total of 31 672 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tretinoin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tretinoin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	600	0	110 089
Type B	0	900	0	118 242
Type C	0	659	56	110 532

The substance/substance group *Tretinoin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 99.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.3333 %)
Type C	100.0000 % (> 99.8899 %)	92.1678 % (> 91.7483 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tretinoin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ornithine aspartate	26.88	—
Tetracaine base	33.64	—
Mepivacaine hydrochloride	44.06	—

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continued from previous page

Substanz	Distance in main model	Distance in second-stage model
Xylometazoline hydrochloride	44.54	—
Ibuprofen	45.02	—
Metoprolol tartrate	46.19	—
Ofloxacin	50.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tretinoin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22574	22574	0.00	51.53
21757	21757	0.00	45.00
21878	21747	12.34	43.27
21747	21747	0.00	43.32
21940	21940	0.00	47.71
22936	21940	2.88	50.21

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Triamcinolone acetonide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20765-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Triamcinolone acetonide; Triamcinoloni acetonidum

Special notes

When selecting the *Triamcinolone acetonide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Triamcinolone acetonide	10	17	504

Second-stage model

For differentiation of the substance/substance group *Triamcinolone acetonide* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Triamcinolone acetonide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Triamcinolone ac...	13256607	21061	100	AR-15-FG-003755-01
Caelo	Triamcinolone ac...	13379921	21587	60	1503634
Euro OTC	Triamcinolone ac...	1303001-02	20910	40	20130815
Euro OTC	Triamcinolone ac...	1211013-02	21072	30	20130417
Euro OTC	Triamcinolone ac...	1508008	21883	60	20150902*
Euro OTC	Triamcinolone ac...	1601021	22313	45	20160119*
Euro OTC	Triamcinolone ac...	1605010	22572	40	20160531*
Euro OTC	Triamcinolone ac...	1605010	22572SI	25	20160531*
Euro OTC	Triamcinolone ac...	1608005	22752	40	20160906*
Euro OTC	Triamcinolone ac...	1608005	22752SI	22	20160906*
Fagron	Triamcinolone ac...	12E15-N03	20765	60	1412051
Fagron	Triamcinolone ac...	15C19-B06-308572	21962	60	20150402

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 582 spectra of 12 reference samples from the substance/substance group *Triamcinolone acetonide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 10 different batches.
- 110 107 spectra from a total of 1956 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples:

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1198 spectra of 36 reference samples from the substance/substance group *Triamcinolone acetonide*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Triamcinolone acetonide	12301505	20769	60
Caelo	Triamcinolone acetonide	160945	22473	60
Caelo	Triamcinolone acetonide	171206	23330	40
Caelo	Triamcinolone acetonide	181002	24016	40
Caelo	Triamcinolone acetonide	190619	24509	40
Euro OTC	Triamcinolone acetonide	1612014	22978	40
Euro OTC	Triamcinolone acetonide	1703037	23393	40
Euro OTC	Triamcinolone acetonide	1706013	23557	40
Euro OTC	Triamcinolone acetonide	1710002	23694	40
Euro OTC	Triamcinolone acetonide	1801020	23883	40
Euro OTC	Triamcinolone acetonide	1805001-01	24191	40
Euro OTC	Triamcinolone acetonide	1810015	24333	40
Euro OTC	Triamcinolone acetonide	1903015	24629	40
Euro OTC	Triamcinolone acetonide	1907044	24842	40
Euro OTC	Triamcinolone acetonide	2001017	25115	40
Euro OTC	Triamcinolone acetonide	2002047	25117	40
Fagron	Triamcinolone acetonide	13C13-N20	21043	60
Caelo	Triamcinolone acetonide	160945	22473SI	40
Caelo	Triamcinolone acetonide	171206	23330SI	20
Caelo	Triamcinolone acetonide	171206	23343	40
Caelo	Triamcinolone acetonide	171206	23343SI	20
Caelo	Triamcinolone acetonide	181002	24016SI	20
Caelo	Triamcinolone acetonide	190619	24509SI	20
Euro OTC	Triamcinolone acetonide	1508008	21883SI [†]	30
Euro OTC	Triamcinolone acetonide	1612014	22978SI	29
Euro OTC	Triamcinolone acetonide	1703037	23393SI	20
Euro OTC	Triamcinolone acetonide	1706013	23557SI	20
Euro OTC	Triamcinolone acetonide	1710002	23694SI	20
Euro OTC	Triamcinolone acetonide	1801020	23883SI	20
Euro OTC	Triamcinolone acetonide	1805001-01	24191SI	20
Euro OTC	Triamcinolone acetonide	1810015	24333SI	20
Euro OTC	Triamcinolone acetonide	1903015	24629SI	20
Euro OTC	Triamcinolone acetonide	1907044	24842SI	20
Euro OTC	Triamcinolone acetonide	2001017	25115SI	40
Euro OTC	Triamcinolone acetonide	2002047	25117SI	20
Fagron	Triamcinolone acetonide	15C19-B06-308572	21962SI [†]	19

- 117944 spectra from a total of 2401 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2564 spectra from 609 *Apo-Ident* customers from 530 batches from the substance/substance group *Triamcinolone acetonide*.
- Among them are spectra of independent samples from 504 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
A.H. 07.05.13 ek: 7,25EUR	Triamcinolone acetonide	1211013-02	1
A.H.D.	Triamcinolone acetonide	12301508	1
AHD	Triamcinolone acetonide	14355711	1
AHD	Triamcinolone acetonide	APU0544/315240T	1
AHD 03.03.2015	Triamcinolone acetonide	NT1430M	1
AHD 06.03.15 9,47	Triamcinolone acetonide	14355102	2
AHD 22.12.16 EK 29,74	Triamcinolone acetonide	16D14B11322136	1
Caelo	Triamcinolone acetonide	15430103	6
AHD/Hedinger	Triamcinolone acetonide	15233902	1
Caelo	Triamcinolone acetonide	17057901	8
Alliance Healthcare	Triamcinolone acetonide	13C13-N20	2
Euro OTC	Triamcinolone acetonide	180500101	1
Fagron	Triamcinolone acetonide	13K15-B31-289027	6
Allianz Healthcare	Triamcinolone acetonide	16080005-01	1
almirall/gehe	Triamcinolone acetonide	17120607	4
Anzag	Triamcinolone acetonide	1303001-02	1
Anzag	Triamcinolone acetonide	14355103	1
Anzag	Triamcinolone acetonide	14355711	1
Anzag	Triamcinolone acetonide	1605010-01	1
Anzag	Triamcinolone acetonide	17120605	1
Fagron	Triamcinolone acetonide	120600801	1
Caelo	Triamcinolone acetonide	13124805	7
apo ident	Triamcinolone acetonide	1612014-01	1
apoident	Triamcinolone acetonide	1508008-01	1
Apomix/Phönix	Triamcinolone acetonide	13k15-b31-289029	2
Apotheke Mildenau	Triamcinolone acetonide	13C13-N20	1
Audor Pharma	Triamcinolone acetonide	APU0544/3162705	1
Audor Pharma	Triamcinolone acetonide	U0544/315240T	1
Audor Pharma	Triamcinolone acetonide	APU0544/315240T	3
Audor Pharma	Triamcinolone acetonide	15240T	1
Audor Pharma	Triamcinolone acetonide	APU0544/31524T	1
Audor Pharma	Triamcinolone acetonide	APU0544/316270T	2
Audor Pharma	Triamcinolone acetonide	APNET180403T	1
Audor Pharma	Triamcinolone acetonide	APU0544/317171T	1
Berkel AHK	Triamcinolone acetonide	14355101	3
Bombas/Sanac	Triamcinolone acetonide	16094506	1
Bombastus	Triamcinolone acetonide	13K15-B31	2
Bombastus	Triamcinolone acetonide	17120610	1
Caelo	Triamcinolone acetonide	14G23_B07_2976618	1
Caelo	Triamcinolone acetonide	160800501	1
Caelo	Triamcinolone acetonide	10220341	1
Caelo	Triamcinolone acetonide	1107212516	1
Caelo	Triamcinolone acetonide	11267721	2
Caelo	Triamcinolone acetonide	11267707	4
Caelo	Triamcinolone acetonide	1209040-01	1
Caelo	Triamcinolone acetonide	12173710	5
Caelo	Triamcinolone acetonide	9364429	2
Caelo	Triamcinolone acetonide	12301501	4
Caelo	Triamcinolone acetonide	12/10-N09	3
Caelo	Triamcinolone acetonide	12301508	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone acetonide	12301503	1
Caelo	Triamcinolone acetonide	12301504	1
Caelo	Triamcinolone acetonide	12301509	4
Caelo	Triamcinolone acetonide	11267705	1
Caelo	Triamcinolone acetonide	2513M02516	1
Caelo	Triamcinolone acetonide	12301510	4
Caelo	Triamcinolone acetonide	12301518	4
Caelo	Triamcinolone acetonide	9081305	1
Caelo	Triamcinolone acetonide	13124804	14
Caelo	Triamcinolone acetonide	13124803	2
Caelo	Triamcinolone acetonide	1811211	1
Caelo	Triamcinolone acetonide	1312407	1
Caelo	Triamcinolone acetonide	3041206	1
Caelo	Triamcinolone acetonide	15233906	16
Caelo	Triamcinolone acetonide	13124811	4
Caelo	Triamcinolone acetonide	13379903	2
Caelo	Triamcinolone acetonide	6051401	1
Caelo	Triamcinolone acetonide	13379913	4
Caelo	Triamcinolone acetonide	13379912	10
Caelo	Triamcinolone acetonide	14188304	4
Caelo	Triamcinolone acetonide	13379919	1
Caelo	Triamcinolone acetonide	14188303	4
Caelo	Triamcinolone acetonide	14255104	1
Caelo	Triamcinolone acetonide	13379922	1
Caelo	Triamcinolone acetonide	12301505	1
Caelo	Triamcinolone acetonide	12301502	1
Caelo	Triamcinolone acetonide	13K15-B31-289031	1
Caelo	Triamcinolone acetonide	14355102	17
Caelo	Triamcinolone acetonide	14355711	8
Caelo	Triamcinolone acetonide	15233901	13
Caelo	Triamcinolone acetonide	8681	1
Caelo	Triamcinolone acetonide	15C19-B06-308571	1
Caelo	Triamcinolone acetonide	14355706	1
Caelo	Triamcinolone acetonide	12031601	1
Caelo	Triamcinolone acetonide	310320161	1
Caelo	Triamcinolone acetonide	15233908	2
Caelo	Triamcinolone acetonide	15G31-B07-313597	1
Caelo	Triamcinolone acetonide	15L21-B03-316123	1
Caelo	Triamcinolone acetonide	5430105	1
Caelo	Triamcinolone acetonide	15430102	1
Caelo	Triamcinolone acetonide	160501001	1
Caelo	Triamcinolone acetonide	15430106	5
Caelo	Triamcinolone acetonide	15430108	9
Caelo	Triamcinolone acetonide	16094501	10
Caelo	Triamcinolone acetonide	16092504	20
Caelo	Triamcinolone acetonide	1608005-01	5
Caelo	Triamcinolone acetonide	1612014	1
Caelo	Triamcinolone acetonide	17057903	2
Caelo	Triamcinolone acetonide	1703037	1
Caelo	Triamcinolone acetonide	170303701	2
Caelo	Triamcinolone acetonide	17057910	1
Caelo	Triamcinolone acetonide	17120603	18
Caelo	Triamcinolone acetonide	17120605	9
Caelo	Triamcinolone acetonide	17120604	7
Caelo	Triamcinolone acetonide	17057909	2
Caelo	Triamcinolone acetonide	17120619	7
Caelo	Triamcinolone acetonide	17120610	11
Caelo	Triamcinolone acetonide	17120607	4
Caelo	Triamcinolone acetonide	16D14-B11-321318	1
Caelo	Triamcinolone acetonide	17358302	25

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone acetonide	17358305	23
Caelo	Triamcinolone acetonide	17356306	1
Caelo	Triamcinolone acetonide	18010202-01	1
Caelo	Triamcinolone acetonide	29091806	1
Caelo	Triamcinolone acetonide	18100213	7
Caelo	Triamcinolone acetonide	18100203	3
Caelo	Triamcinolone acetonide	18100210	12
Caelo	Triamcinolone acetonide	18100207	1
Caelo	Triamcinolone acetonide	18F14-B01-351889	1
Caelo	Triamcinolone acetonide	18100220	7
Caelo	Triamcinolone acetonide	18100222	6
Caelo	Triamcinolone acetonide	18100217	3
Caelo	Triamcinolone acetonide	19120211	2
Caelo	Triamcinolone acetonide	191202006	1
Caelo	Triamcinolone acetonide	1210-n09	1
Caelo	Triamcinolone acetonide	11267704	1
Caelo	Triamcinolone acetonide	16094514	16
Caelo	Triamcinolone acetonide	180500102	1
Caelo	Triamcinolone acetonide	1801020-01	4
Caelo	Triamcinolone acetonide	18100209	7
Caelo	Triamcinolone acetonide	18F14-B01-352343	1
Caelo	Triamcinolone acetonide	1912208	1
Caelo	Triamcinolone acetonide	14355103	12
Caelo	Triamcinolone acetonide	13K14-B04-289033	2
Caelo	Triamcinolone acetonide	14355702	11
Caelo	Triamcinolone acetonide	15233905	6
Caelo	Triamcinolone acetonide	1706601-01	1
Caelo	Triamcinolone acetonide	1805001-02	2
Caelo	Triamcinolone acetonide	13124806	2
Caelo	Triamcinolone acetonide	12301507	8
Caelo	Triamcinolone acetonide	17C09-B01-340174	1
Caelo	Triamcinolone acetonide	1110005-01	1
Caelo	Triamcinolone acetonide	17H03-B12-345552	1
Caelo	Triamcinolone acetonide	170324T1612014-01	1
Caelo	Triamcinolone acetonide	17358302-T20181115Ma	1
Caelo	Triamcinolone acetonide	120904002	1
Caelo	Triamcinolone acetonide	13124808	13
Caelo	Triamcinolone acetonide	1706013-01	3
Caelo	Triamcinolone acetonide	42(18100213)	1
Caelo	Triamcinolone acetonide	17H03-B12-343457	1
Caelo	Triamcinolone acetonide	17057908	17
Caelo	Triamcinolone acetonide	16079502	1
Caelo	Triamcinolone acetonide	1504007-01	1
Caelo	Triamcinolone acetonide	1201506	1
Caelo	Triamcinolone acetonide	15C19-B06-308573	1
Caelo	Triamcinolone acetonide	18C15-B05-349087	1
Caelo	Triamcinolone acetonide	3282	1
Caelo	Triamcinolone acetonide	3340	1
Caelo	Triamcinolone acetonide	14233904	1
Caelo	Triamcinolone acetonide	1508008-01	2
Caelo	Triamcinolone acetonide	13256604	6
Caelo	Triamcinolone acetonide	17120606	13
Caelo	Triamcinolone acetonide	18100205	6
Caelo	Triamcinolone acetonide	16094504	5
Caelo	Triamcinolone acetonide	16K07-B06-329447	1
Caelo	Triamcinolone acetonide	17057905	13
Caelo	Triamcinolone acetonide	11267720	1
Caelo	Triamcinolone acetonide	12301515	12
Caelo	Triamcinolone acetonide	1303001-02	1
Caelo	Triamcinolone acetonide	1355101	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone acetonide	160102101	1
Caelo	Triamcinolone acetonide	17120618	6
Caelo	Triamcinolone acetonide	12173704	2
Caelo	Triamcinolone acetonide	13e15-n03	1
Caelo	Triamcinolone acetonide	13124807	11
Caelo	Triamcinolone acetonide	1206008-01	1
Caelo	Triamcinolone acetonide	13256608	2
Caelo	Triamcinolone acetonide	13379911	1
Caelo	Triamcinolone acetonide	14355709	2
Caelo	Triamcinolone acetonide	1230517/16094502	1
Caelo	Triamcinolone acetonide	1120717/16094502	1
Caelo	Triamcinolone acetonide	18F14B01355979	1
Caelo	Triamcinolone acetonide	19120209	1
Caelo	Triamcinolone acetonide	11267710	2
Caelo	Triamcinolone acetonide	15430105	6
Caelo	Triamcinolone acetonide	16094512	5
Caelo	Triamcinolone acetonide	1710002-01	1
Caelo	Triamcinolone acetonide	1720608	1
Caelo	Triamcinolone acetonide	13124801	6
Caelo	Triamcinolone acetonide	1211013-01	1
Caelo	Triamcinolone acetonide	15233903	26
Caelo	Triamcinolone acetonide	15233902	23
Caelo	Triamcinolone acetonide	13124810	2
Caelo	Triamcinolone acetonide	14188302	5
Caelo	Triamcinolone acetonide	14355104	2
Caelo	Triamcinolone acetonide	14355703	3
Caelo	Triamcinolone acetonide	15233904	13
Caelo	Triamcinolone acetonide	14355701	1
Caelo	Triamcinolone acetonide	1504007-02	1
Caelo	Triamcinolone acetonide	1605010-01	1
Caelo	Triamcinolone acetonide	16094511	16
Caelo	Triamcinolone acetonide	1504007-2	1
Caelo	Triamcinolone acetonide	1530102	1
Caelo	Triamcinolone acetonide	17057906	13
Caelo	Triamcinolone acetonide	16D14-B11	1
Caelo	Triamcinolone acetonide	17120608	10
Caelo	Triamcinolone acetonide	18100226	4
Caelo	Triamcinolone acetonide	180102001	1
Caelo	Triamcinolone acetonide	4613E2516	1
Caelo	Triamcinolone acetonide	13E15-N03	2
Caelo	Triamcinolone acetonide	13124809	1
Caelo	Triamcinolone acetonide	1514Q2516	1
Caelo	Triamcinolone acetonide	13K15-B31-289027	2
Caelo	Triamcinolone acetonide	16094506	6
Caelo	Triamcinolone acetonide	1735802	1
Caelo	Triamcinolone acetonide	18100204	7
Caelo	Triamcinolone acetonide	19120208	7
Caelo	Triamcinolone acetonide	19120207	2
Caelo	Triamcinolone acetonide	13256603	1
Caelo	Triamcinolone acetonide	12301506	1
Caelo	Triamcinolone acetonide	13379904	6
Caelo	Triamcinolone acetonide	13379914	6
Caelo	Triamcinolone acetonide	12173703	1
Caelo	Triamcinolone acetonide	14355712	7
Caelo	Triamcinolone acetonide	1508008-02	1
Caelo	Triamcinolone acetonide	15L21-B03-318663	1
Caelo	Triamcinolone acetonide	15G31-B07-314045	1
Caelo	Triamcinolone acetonide	15430107	13
Caelo	Triamcinolone acetonide	1612014-01	8
Caelo	Triamcinolone acetonide	17057902	11

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone acetonide	17057907	5
Caelo	Triamcinolone acetonide	17128606	1
Caelo	Triamcinolone acetonide	17120620	7
Caelo	Triamcinolone acetonide	17358303	5
Caelo	Triamcinolone acetonide	17358304	7
Caelo	Triamcinolone acetonide	18100206	5
Caelo	Triamcinolone acetonide	16K07-B06-332102	1
Caelo	Triamcinolone acetonide	18100225	1
Caelo	Triamcinolone acetonide	13I26-N11	1
Caelo	Triamcinolone acetonide	13379905	16
Caelo	Triamcinolone acetonide	14355704	3
Caelo	Triamcinolone acetonide	16094513	1
Caelo	Triamcinolone acetonide	18100221	7
Caelo	Triamcinolone acetonide	17120611	23
Caelo	Triamcinolone acetonide	16094507	3
Caesar & Loretz GmbH	Triamcinolone acetonide	17057906	1
Caesar & Loretz GmbH	Triamcinolone acetonide	17057907	1
Caesar & Loretz GmbH	Triamcinolone acetonide	17120610	1
Caesar & Loretz GmbH	Triamcinolone acetonide	17358305	1
Caesar & Loretz GmbH	Triamcinolone acetonide	175358305	1
Caesar & Loretz GmbH	Triamcinolone acetonide	17358309	1
Caesar & Loretz GmbH	Triamcinolone acetonide	18100203	2
Caesar & Loretz GmbH	Triamcinolone acetonide	18100213	1
Caesar & Loretz GmbH	Triamcinolone acetonide	18100221	1
Caesar & Loretz GmbH	Triamcinolone acetonide	18100206	2
Caesar & Loretz GmbH	Triamcinolone acetonide	18100218	1
Caesar & Loretz GmbH	Triamcinolone acetonide	17358302	1
Caesar & Loretz GmbH	Triamcinolone acetonide	18100226	1
Caesar & Loretz GmbH	Triamcinolone acetonide	19120208	1
Caesar & Loretz GmbH	Triamcinolone acetonide	19120210	1
Caesar & Loretz GmbH	Triamcinolone acetonide	19120206	1
Caesar & Loretz GmbH	Triamcinolone acetonide	19120209	1
Caesar & Loretz GmbH / ...	Triamcinolone acetonide	19120210	1
Caesar & Loretz GmbH / ...	Triamcinolone acetonide	19120208	1
Caesar & Loretz GmbH / ...	Triamcinolone acetonide	18100221	1
Caesar & Loretz GmbH Hi...	Triamcinolone acetonide	13379905	1
Caesar & Loretz GmbH/ P...	Triamcinolone acetonide	19120208	1
Caesar & Loretz GmbH/Ge...	Triamcinolone acetonide	19120207	1
Caesar & Loretz GmbH/Go...	Triamcinolone acetonide	19120210	1
Caesar & Loretz GmbH/Gö...	Triamcinolone acetonide	18100222	1
Caesar & Loretz GmbH/Mi...	Triamcinolone acetonide	18100210	1
Caesar&lorenz,Phoenix	Triamcinolone acetonide	11267705	1
Caesar&lorenz,Phoenix	Triamcinolone acetonide	12173703	1
Caesar&lorenz,Phoenix	Triamcinolone acetonide	12301502	1
Calo/Sanacorp	Triamcinolone acetonide	16092504	1
Cealo	Triamcinolone acetonide	1907044-01	1
Cealo/Phönix	Triamcinolone acetonide	17057901	1
cesar&lorenz/Phönix	Triamcinolone acetonide	13124801	1
Dr. Wolff	Triamcinolone acetonide	1612014-01	1
Ebert/Euo	Triamcinolone acetonide	1612014-01	1
Eigen/Defektur	Triamcinolone acetonide	U0544/113530	1
E-plus	Triamcinolone acetonide	17120610	2
Eurho	Triamcinolone acetonide	1805001-02	1
EuRho	Triamcinolone acetonide	1403009-02	1
EuRho	Triamcinolone acetonide	150800-08-02	1
EuRho	Triamcinolone acetonide	1508008-02	2
EuRho	Triamcinolone acetonide	NW2518M	1
EuRho	Triamcinolone acetonide	1703037-01	1
EuRho	Triamcinolone acetonide	1706013-01	2
EuRho / Phoenix	Triamcinolone acetonide	1612014-01	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Spangropharm	Triamcinolone acetonide	1209040-02	1
EuRho/ Sanacorp	Triamcinolone acetonide	1703037-01	1
EuRho/Noweda	Triamcinolone acetonide	1601021-01	1
EuRho/Noweda	Triamcinolone acetonide	1710002-01	1
EuRho/Phoenix	Triamcinolone acetonide	1403009-02	1
EuRho/Phönix	Triamcinolone acetonide	1211013-01	1
EuRho/Phönix	Triamcinolone acetonide	1307043-02	1
EuRho/Phönix	Triamcinolone acetonide	1407044-01	1
Eurho/Sanacorp	Triamcinolone acetonide	1710002-01	1
euro	Triamcinolone acetonide	1211013-02	1
Euro	Triamcinolone acetonide	1303001-02	1
Euro / Noweda	Triamcinolone acetonide	1612014-01	1
Euro OTC	Triamcinolone acetonide	8700	1
Euro OTC	Triamcinolone acetonide	2772	1
Euro OTC	Triamcinolone acetonide	2898	1
Euro OTC	Triamcinolone acetonide	150400701	2
Euro OTC	Triamcinolone acetonide	181001501	1
Euro OTC	Triamcinolone acetonide	20130912-5	1
Euro OTC	Triamcinolone acetonide	1013I-02516	1
Euro OTC	Triamcinolone acetonide	121113-02	1
Euro OTC	Triamcinolone acetonide	1307043-03	1
Euro OTC	Triamcinolone acetonide	3051402	1
Euro OTC	Triamcinolone acetonide	17061406	1
Euro OTC	Triamcinolone acetonide	26081405	1
Euro OTC	Triamcinolone acetonide	1407044-01	9
Euro OTC	Triamcinolone acetonide	31101414	1
Euro OTC	Triamcinolone acetonide	29011503	1
Euro OTC	Triamcinolone acetonide	1412013-01	13
Euro OTC	Triamcinolone acetonide	141213-02	1
Euro OTC	Triamcinolone acetonide	1504007-01	9
Euro OTC	Triamcinolone acetonide	1504007-02	17
Euro OTC	Triamcinolone acetonide	29081501	1
Euro OTC	Triamcinolone acetonide	1605010-01	37
Euro OTC	Triamcinolone acetonide	161006T	1
Euro OTC	Triamcinolone acetonide	15121-b03-316123	1
Euro OTC	Triamcinolone acetonide	15430103	1
Euro OTC	Triamcinolone acetonide	15081701	1
Euro OTC	Triamcinolone acetonide	161214-01	1
Euro OTC	Triamcinolone acetonide	15111740	1
Euro OTC	Triamcinolone acetonide	1706013	1
Euro OTC	Triamcinolone acetonide	170601301	4
Euro OTC	Triamcinolone acetonide	26011804	1
Euro OTC	Triamcinolone acetonide	1706079-01	1
Euro OTC	Triamcinolone acetonide	1710002-1	1
Euro OTC	Triamcinolone acetonide	8031803	1
Euro OTC	Triamcinolone acetonide	17100002-01	1
Euro OTC	Triamcinolone acetonide	1801020-01	43
Euro OTC	Triamcinolone acetonide	5051816	1
Euro OTC	Triamcinolone acetonide	23061808	1
Euro OTC	Triamcinolone acetonide	15121806	1
Euro OTC	Triamcinolone acetonide	12G6008-01	1
Euro OTC	Triamcinolone acetonide	1903015-15	1
Euro OTC	Triamcinolone acetonide	1601021-01	30
Euro OTC	Triamcinolone acetonide	1206008-01	5
Euro OTC	Triamcinolone acetonide	150800802	2
Euro OTC	Triamcinolone acetonide	1608005-01	36
Euro OTC	Triamcinolone acetonide	1706013-01	51
Euro OTC	Triamcinolone acetonide	B0544/111404	1
Euro OTC	Triamcinolone acetonide	1211013-01	4
Euro OTC	Triamcinolone acetonide	15042014A	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Triamcinolone acetonide	1407044-02	15
Euro OTC	Triamcinolone acetonide	3022015A	1
Euro OTC	Triamcinolone acetonide	141201301	1
Euro OTC	Triamcinolone acetonide	APB0544/112020T	1
Euro OTC	Triamcinolone acetonide	28041728	1
Euro OTC	Triamcinolone acetonide	NW2518M	1
Euro OTC	Triamcinolone acetonide	171002-01	2
Euro OTC	Triamcinolone acetonide	11801020-01	1
Euro OTC	Triamcinolone acetonide	1110005-01	2
Euro OTC	Triamcinolone acetonide	111005-01	1
Euro OTC	Triamcinolone acetonide	NV0635M	1
Euro OTC	Triamcinolone acetonide	80616-5	1
Euro OTC	Triamcinolone acetonide	16D14-B11-322136	1
Euro OTC	Triamcinolone acetonide	1805001-01	16
Euro OTC	Triamcinolone acetonide	1805001	1
Euro OTC	Triamcinolone acetonide	1903015-01	18
Euro OTC	Triamcinolone acetonide	1907044-01	11
Euro OTC	Triamcinolone acetonide	1112023-02	6
Euro OTC	Triamcinolone acetonide	1112023-01	1
Euro OTC	Triamcinolone acetonide	1209040-01	4
Euro OTC	Triamcinolone acetonide	1508008-02	15
Euro OTC	Triamcinolone acetonide	15L21-B03-316123	2
Euro OTC	Triamcinolone acetonide	171302-01	1
Euro OTC	Triamcinolone acetonide	PT49	1
Euro OTC	Triamcinolone acetonide	1303001-01	5
Euro OTC	Triamcinolone acetonide	15041007-02	1
Euro OTC	Triamcinolone acetonide	171212T/1703037-01	1
Euro OTC	Triamcinolone acetonide	180102001	2
Euro OTC	Triamcinolone acetonide	1307043-01	16
Euro OTC	Triamcinolone acetonide	170303701	1
Euro OTC	Triamcinolone acetonide	1805001-02	10
Euro OTC	Triamcinolone acetonide	14030009-01	2
Euro OTC	Triamcinolone acetonide	15233906	2
Euro OTC	Triamcinolone acetonide	112014-01	1
Euro OTC	Triamcinolone acetonide	181016181	1
Euro OTC	Triamcinolone acetonide	180500102	1
Euro OTC	Triamcinolone acetonide	1403009-02	13
Euro OTC	Triamcinolone acetonide	14120130	1
Euro OTC	Triamcinolone acetonide	15404007-01	1
Euro OTC	Triamcinolone acetonide	181020-1	1
Euro OTC	Triamcinolone acetonide	190704401	1
Euro OTC	Triamcinolone acetonide	13030001-01	1
Euro OTC	Triamcinolone acetonide	14188304	1
Euro OTC	Triamcinolone acetonide	171613-01	1
euro/ Anzag	Triamcinolone acetonide	3315I02516	1
Euro/Gehe	Triamcinolone acetonide	1612014-01	1
Euro/Gehe	Triamcinolone acetonide	1703037-01	1
Euro/Noweda	Triamcinolone acetonide	161201401	1
Euro OTC	Triamcinolone acetonide	1703037-01	41
Euro/Phönix	Triamcinolone acetonide	1805401	1
Euro/Phönix	Triamcinolone acetonide	1907044	1
euroct/gehe	Triamcinolone acetonide	1403009	1
euroct/gehe	Triamcinolone acetonide	1403009-02	1
EuroOCT/Gehe	Triamcinolone acetonide	1710002-01	2
Euro OTC	Triamcinolone acetonide	1508008-01	15
Euro OTC	Triamcinolone acetonide	130704301	1
Euro OTC	Triamcinolone acetonide	14030009-02	1
Euro OTC	Triamcinolone acetonide	1612014-01	54
Euro OTC	Triamcinolone acetonide	1602005-01	1
Euro OTC	Triamcinolone acetonide	160501001	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Triamcinolone acetonide	1412013-02	8
Euro OTC	Triamcinolone acetonide	1209040-02	2
Euro OTC	Triamcinolone acetonide	1403009-01	7
Euro OTC	Triamcinolone acetonide	1801020-1	1
Euro OTC	Triamcinolone acetonide	1810015-01	38
Euro OTC	Triamcinolone acetonide	190301501	1
Euro OTC	Triamcinolone acetonide	1307043-02	14
Euro OTC	Triamcinolone acetonide	15233904	1
Europharm/Otto	Triamcinolone acetonide	1206008-01	1
Europharm/Otto	Triamcinolone acetonide	1209040-02	1
Europharm/Sanacorp	Triamcinolone acetonide	B0544/111040	2
Europharm/Sanacorp	Triamcinolone acetonide	1211013-01	3
Euro OTC	Triamcinolone acetonide	1710002-01	43
Fagron	Triamcinolone acetonide	4111408	1
Fagron	Triamcinolone acetonide	14G23-B07	1
Fagron	Triamcinolone acetonide	17C09-B01	3
Fagron	Triamcinolone acetonide	18c15-b05-350263	1
Fagron	Triamcinolone acetonide	11K11-N10	6
Fagron	Triamcinolone acetonide	12B08-N01	8
Fagron	Triamcinolone acetonide	5061205	1
Fagron	Triamcinolone acetonide	NS0571M	5
Fagron	Triamcinolone acetonide	NS0571M	1
Fagron	Triamcinolone acetonide	13121201	1
Fagron	Triamcinolone acetonide	1210-N09	1
Fagron	Triamcinolone acetonide	12E15/N03	1
Fagron	Triamcinolone acetonide	12I10-N09	4
Fagron	Triamcinolone acetonide	12I10-N09	3
Fagron	Triamcinolone acetonide	20031302	1
Fagron	Triamcinolone acetonide	9041305	1
Fagron	Triamcinolone acetonide	13C13-20	1
Fagron	Triamcinolone acetonide	5061303	1
Fagron	Triamcinolone acetonide	NS2236M	1
Fagron	Triamcinolone acetonide	13E15-N03	44
Fagron	Triamcinolone acetonide	13E15N03	3
Fagron	Triamcinolone acetonide	12B08N01	1
Fagron	Triamcinolone acetonide	5121302	1
Fagron	Triamcinolone acetonide	16011407	1
Fagron	Triamcinolone acetonide	12301503	1
Fagron	Triamcinolone acetonide	13K14-B04-289033	10
Fagron	Triamcinolone acetonide	14G23-B07-297620	6
Fagron	Triamcinolone acetonide	14K24N-N01	1
Fagron	Triamcinolone acetonide	411082-1-P	1
Fagron	Triamcinolone acetonide	13021408	1
Fagron	Triamcinolone acetonide	13I26-N11	13
Fagron	Triamcinolone acetonide	13I26-N26	1
Fagron	Triamcinolone acetonide	13/26-N11	6
Fagron	Triamcinolone acetonide	13E15-N03	1
Fagron	Triamcinolone acetonide	13K15-B31	7
Fagron	Triamcinolone acetonide	1326-N11	1
Fagron	Triamcinolone acetonide	13126-N11	1
Fagron	Triamcinolone acetonide	NT0770M	1
Fagron	Triamcinolone acetonide	NT1094M	1
Fagron	Triamcinolone acetonide	13K14-B04-289032	5
Fagron	Triamcinolone acetonide	14F30-B01-296287	4
Fagron	Triamcinolone acetonide	14F30-B01	2
Fagron	Triamcinolone acetonide	7041501	1
Fagron	Triamcinolone acetonide	14F30B01	1
Fagron	Triamcinolone acetonide	14G23-B07-297618	4
Fagron	Triamcinolone acetonide	1412013-01	1
Fagron	Triamcinolone acetonide	15B02-B03	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triamcinolone acetonide	13I26N11	1
Fagron	Triamcinolone acetonide	15B02-B03-303830	7
Fagron	Triamcinolone acetonide	15B02-B03-303828	3
Fagron	Triamcinolone acetonide	14k14-B05-302887	1
Fagron	Triamcinolone acetonide	1508008-01	2
Fagron	Triamcinolone acetonide	15C19-B06-308573	7
Fagron	Triamcinolone acetonide	15C19-B06-309194	2
Fagron	Triamcinolone acetonide	1531-07-313596	1
Fagron	Triamcinolone acetonide	15G31-B07-313597	5
Fagron	Triamcinolone acetonide	15G31-B07-314045	5
Fagron	Triamcinolone acetonide	15G31-B07	2
Fagron	Triamcinolone acetonide	15G31B07	2
Fagron	Triamcinolone acetonide	15B02-B03-303828	1
Fagron	Triamcinolone acetonide	16B04-B07-318957	6
Fagron	Triamcinolone acetonide	12/-N09	1
Fagron	Triamcinolone acetonide	15L21-B03	1
Fagron	Triamcinolone acetonide	15L21-B03-318663	3
Fagron	Triamcinolone acetonide	16B04-B07-318664	5
Fagron	Triamcinolone acetonide	16B04-B07	4
Fagron	Triamcinolone acetonide	1608005-01	1
Fagron	Triamcinolone acetonide	16D14-B11	2
Fagron	Triamcinolone acetonide	16D14-B11-325479	5
Fagron	Triamcinolone acetonide	16B04	1
Fagron	Triamcinolone acetonide	1612014-01	1
Fagron	Triamcinolone acetonide	16B04-B07318664	1
Fagron	Triamcinolone acetonide	16K07-B06	3
Fagron	Triamcinolone acetonide	16D14-B11-328167	12
Fagron	Triamcinolone acetonide	16K07-B06-332101	6
Fagron	Triamcinolone acetonide	16D14-B11_322158	1
Fagron	Triamcinolone acetonide	16K07-B06-332102	4
Fagron	Triamcinolone acetonide	17C09-B01-337464	2
Fagron	Triamcinolone acetonide	17C09-B01-334196	4
Fagron	Triamcinolone acetonide	17C09-B01-334197	4
Fagron	Triamcinolone acetonide	16K07B06329445	1
Fagron	Triamcinolone acetonide	17C09-B01_337464	1
Fagron	Triamcinolone acetonide	17H03-B12-343458	5
Fagron	Triamcinolone acetonide	17H03-B12-343457	5
Fagron	Triamcinolone acetonide	17c09-b01-340174	1
Fagron	Triamcinolone acetonide	18C15-B05	5
Fagron	Triamcinolone acetonide	18C15-B05-347275	4
Fagron	Triamcinolone acetonide	18C15-B05_348063	1
Fagron	Triamcinolone acetonide	17H03-B12-345553	2
Fagron	Triamcinolone acetonide	18C15-B05-348063	3
Fagron	Triamcinolone acetonide	18C15-B05-350263	2
Fagron	Triamcinolone acetonide	18c15-b05-349087	1
Fagron	Triamcinolone acetonide	18F14-B-351889	1
Fagron	Triamcinolone acetonide	18F14-B01-352630	2
Fagron	Triamcinolone acetonide	17h03-b12-343672	1
Fagron	Triamcinolone acetonide	18K16-B05	3
Fagron	Triamcinolone acetonide	18100221	1
Fagron	Triamcinolone acetonide	18K16-B06-357775	1
Fagron	Triamcinolone acetonide	18K16-B05-359871	1
Fagron	Triamcinolone acetonide	18F14-B01-353255	1
Fagron	Triamcinolone acetonide	17H03-B12	5
Fagron	Triamcinolone acetonide	17H03-B12-343459	1
Fagron	Triamcinolone acetonide	18F14-B01-355724	1
Fagron	Triamcinolone acetonide	18K16-B05-359868	1
Fagron	Triamcinolone acetonide	13K14-B04	4
Fagron	Triamcinolone acetonide	15G31-B07-314046	2
Fagron	Triamcinolone acetonide	NT077oM	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triamcinolone acetonide	Nw0635M	1
Fagron	Triamcinolone acetonide	13k15-b31-289030	1
Fagron	Triamcinolone acetonide	16B04-B07-319471	4
Fagron	Triamcinolone acetonide	16K07-B06-329446	1
Fagron	Triamcinolone acetonide	18K16-B05-361523	1
Fagron	Triamcinolone acetonide	16D14-B11-325480	3
Fagron	Triamcinolone acetonide	18C15-B05-349087	4
Fagron	Triamcinolone acetonide	18F14-B01-352343	2
Fagron	Triamcinolone acetonide	14355104	1
Fagron	Triamcinolone acetonide	16B04-Bo7-318664	1
Fagron	Triamcinolone acetonide	18K16-B05-357775	2
Fagron	Triamcinolone acetonide	NU0930M	1
Fagron	Triamcinolone acetonide	15L21-B03-316123	7
Fagron	Triamcinolone acetonide	14F30-B021-296287	1
Fagron	Triamcinolone acetonide	16K07-B06-333438	3
Fagron	Triamcinolone acetonide	12/10-N09	4
Fagron	Triamcinolone acetonide	289027	1
Fagron	Triamcinolone acetonide	16D14-B11-322136	7
Fagron	Triamcinolone acetonide	17H03-B12-345552	4
Fagron	Triamcinolone acetonide	18F14-B01-351889	3
Fagron	Triamcinolone acetonide	17C09-B01-340173	5
Fagron	Triamcinolone acetonide	16D14-B11-325482	6
Fagron	Triamcinolone acetonide	NT1430M	3
Fagron	Triamcinolone acetonide	1407044-01	1
Fagron	Triamcinolone acetonide	16D14-B11-322135	4
Fagron	Triamcinolone acetonide	17C09-B01-336881	1
Fagron	Triamcinolone acetonide	NS0996M	2
Fagron	Triamcinolone acetonide	13K15-B31-289025	1
Fagron	Triamcinolone acetonide	13K15-B31-289031	6
Fagron	Triamcinolone acetonide	14G23-B07-297620	1
Fagron	Triamcinolone acetonide	16D14-B11-325481	1
Fagron	Triamcinolone acetonide	18F14-B01	2
Fagron	Triamcinolone acetonide	18K16-B05-359867	2
Fagron	Triamcinolone acetonide	3212U-02516(NP)	1
Fagron	Triamcinolone acetonide	NT0487M	1
Fagron	Triamcinolone acetonide	13K15B31289029	1
Fagron	Triamcinolone acetonide	13K14-b04	1
Fagron	Triamcinolone acetonide	14355709	1
Fagron	Triamcinolone acetonide	NX0241M	1
Fagron	Triamcinolone acetonide	18C15B05347275	2
Fagron	Triamcinolone acetonide	18F14-B01-356853	2
Fagron	Triamcinolone acetonide	13e15-n03	1
Fagron	Triamcinolone acetonide	17C09-B01-340174	5
Fagron	Triamcinolone acetonide	16D04-B11-325479	1
Fagron	Triamcinolone acetonide	14G23-B07-297619	2
Fagron	Triamcinolone acetonide	15g31-b07-314046	1
Fagron	Triamcinolone acetonide	15B02-B03-303827	2
Fagron	Triamcinolone acetonide	16-B07-318664	1
Fagron	Triamcinolone acetonide	17H03-B12-343672	5
Fagron	Triamcinolone acetonide	11N11-N10	1
Fagron	Triamcinolone acetonide	18F14-B01-357073	2
Fagron	Triamcinolone acetonide	NY2097M	1
Fagron	Triamcinolone acetonide	11B22-N05	1
Fagron	Triamcinolone acetonide	13C13-N20	14
Fagron	Triamcinolone acetonide	13i26-N11	1
Fagron	Triamcinolone acetonide	15C19-B06-308571	1
Fagron	Triamcinolone acetonide	15G31-B07-313596	6
Fagron	Triamcinolone acetonide	15C19-B06	1
Fagron	Triamcinolone acetonide	16D14-B11-322158	7
Fagron	Triamcinolone acetonide	NW2261M	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triamcinolone acetonide	16K07-B06-329445	4
Fagron	Triamcinolone acetonide	NX1540M	1
Fagron	Triamcinolone acetonide	1703-B12-345553	1
Fagron	Triamcinolone acetonide	ny0485m	1
Fagron	Triamcinolone acetonide	1810015-01	1
Fagron	Triamcinolone acetonide	18C15-B05-348064	1
Fagron	Triamcinolone acetonide	13c13-n20	1
Fagron	Triamcinolone acetonide	14K14-B05-302887	2
Fagron	Triamcinolone acetonide	NV0262M	1
Fagron	Triamcinolone acetonide	15G31-B07-314047	3
Fagron	Triamcinolone acetonide	16D14-B11-321318	3
Fagron	Triamcinolone acetonide	NY0485M	1
Fagron	Triamcinolone acetonide	18F14-B01-355979	1
Fagron	Triamcinolone acetonide	13K15-B31-289029	3
fargon	Triamcinolone acetonide	13C13-N20	1
Fargon	Triamcinolone acetonide	Nu2526M	1
Fargon	Triamcinolone acetonide	15C19-B06-308572	2
Fargon	Triamcinolone acetonide	15C19-B06-308573	1
Fargon/Alliance HC	Triamcinolone acetonide	15B02-B03-303830	1
Fargon/Anzag	Triamcinolone acetonide	13/26-N11	3
Fargon	Triamcinolone acetonide	13/26-N11	1
Farmabios S.p.A./Caesar...	Triamcinolone acetonide	15233901	1
Fiebig	Triamcinolone acetonide	15C19-B06-308571	1
Fiebig	Triamcinolone acetonide	16B04-B07-318957	1
Fiebig	Triamcinolone acetonide	17057902	1
Finteler Apotheke	Triamcinolone acetonide	17057910	1
Gehe	Triamcinolone acetonide	700124-0007	1
Gehe	Triamcinolone acetonide	12E15-N03	1
Gehe	Triamcinolone acetonide	12/10-N09	2
Gehe	Triamcinolone acetonide	12301510	2
Gehe	Triamcinolone acetonide	13E15-N03	2
Gehe	Triamcinolone acetonide	13124805	1
Gehe	Triamcinolone acetonide	13I26-N11	1
Gehe	Triamcinolone acetonide	15B02-B03-303827	1
Gehe	Triamcinolone acetonide	15430102	2
Gehe	Triamcinolone acetonide	160800501	1
Gehe	Triamcinolone acetonide	16094501	1
Gehe	Triamcinolone acetonide	17120610	1
Gehe	Triamcinolone acetonide	18C15-B05	1
Gehe	Triamcinolone acetonide	18100203	1
Gehe	Triamcinolone acetonide	18100206	1
Gehe	Triamcinolone acetonide	18100222	1
Gehe	Triamcinolone acetonide	1903015-01	1
GEHE	Triamcinolone acetonide	1605010-01	1
GEHE	Triamcinolone acetonide	16K07-B06-332103	1
GEHE	Triamcinolone acetonide	1706013-01	1
GEHE	Triamcinolone acetonide	1710002-01	1
GEHE	Triamcinolone acetonide	17358303	1
GEHE	Triamcinolone acetonide	18100206	1
GEHE	Triamcinolone acetonide	18100225	2
Caelo	Triamcinolone acetonide	16094505	2
Caelo	Triamcinolone acetonide	31117-1/16094502	1
Caelo	Triamcinolone acetonide	1040417	1
Caelo	Triamcinolone acetonide	17120606/1211117	1
Caelo	Triamcinolone acetonide	12173707	5
Gehe/EuRo	Triamcinolone acetonide	1605010-01	1
Gehe/EuRo	Triamcinolone acetonide	1801020-01	1
Euro OTC	Triamcinolone acetonide	1703037	3
Fagron	Triamcinolone acetonide	13k14-B04-289032	1
Fagron	Triamcinolone acetonide	16D14_B11_328167	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triamcinolone acetonide	16D14B11325479	1
Gehe/Fragon	Triamcinolone acetonide	16D14-B11-325479	1
Gehe/Phönix	Triamcinolone acetonide	1209040-02	1
Caelo	Triamcinolone acetonide	14G23-B07-297619	1
Klenk	Triamcinolone acetonide	1504007-02	1
Hirsch	Triamcinolone acetonide	12I10-N09	2
Ichtyol/Gehe	Triamcinolone acetonide	15430102	3
Jenne	Triamcinolone acetonide	1805001-01	2
Jenne	Triamcinolone acetonide	18C15-B05-347275	1
Caelo	Triamcinolone acetonide	13K15-B31-289029	1
Kehr	Triamcinolone acetonide	1057902	1
Klenk	Triamcinolone acetonide	NS1680M	1
Fagron	Triamcinolone acetonide	17C-09-B01-334197	1
Fagron	Triamcinolone acetonide	15G31B07313597	1
Martinus-Apotheke	Triamcinolone acetonide	13379905	1
Midas	Triamcinolone acetonide	16094511	1
Midas	Triamcinolone acetonide	17H03-B12-343457	1
Midas Göttingen	Triamcinolone acetonide	16094504	1
Newchem	Triamcinolone acetonide	1303001-02	1
NEWCHEM / Sanacorp	Triamcinolone acetonide	15040007-01	1
Newchem S. p. A. / Noweda	Triamcinolone acetonide	17120608	1
Newchem S.P.A	Triamcinolone acetonide	1508008-02	1
NEWCHEM S.P.A.	Triamcinolone acetonide	NV0994M	1
Newchem S.p.A./Caesar &...	Triamcinolone acetonide	1543015	1
Newchem Spa (site)	Triamcinolone acetonide	16K07-B06-332102	1
Newchem/ Noweda	Triamcinolone acetonide	1403009-01	1
Newchem/AHD	Triamcinolone acetonide	1407044-02	1
Newchem/Fiebig	Triamcinolone acetonide	1605010-01	1
Newchem/Kehr	Triamcinolone acetonide	1407044-01	1
Newchem/Noweda	Triamcinolone acetonide	15C19-B06-308573	1
Newchem/Phönix	Triamcinolone acetonide	1810015-01	1
Noveda	Triamcinolone acetonide	12301518	1
noweda	Triamcinolone acetonide	13256604	1
Noweda	Triamcinolone acetonide	1112023-02	1
Noweda	Triamcinolone acetonide	12E15-N03	1
Noweda	Triamcinolone acetonide	12301501	1
Noweda	Triamcinolone acetonide	12301509	1
Noweda	Triamcinolone acetonide	13K15-B31-289029	1
Noweda	Triamcinolone acetonide	1407044-01	1
Noweda	Triamcinolone acetonide	14355708	1
Noweda	Triamcinolone acetonide	14355103	1
Noweda	Triamcinolone acetonide	15233902	1
Noweda	Triamcinolone acetonide	15233903	1
Noweda	Triamcinolone acetonide	1605010-01	1
Noweda	Triamcinolone acetonide	16094514	1
Noweda	Triamcinolone acetonide	1608005-01	1
Noweda	Triamcinolone acetonide	17057908	1
Noweda	Triamcinolone acetonide	17057905	2
Noweda	Triamcinolone acetonide	1703037-01	2
Noweda	Triamcinolone acetonide	17120606	2
Noweda	Triamcinolone acetonide	17120611	1
Noweda	Triamcinolone acetonide	18100221	1
Noweda	Triamcinolone acetonide	181000226	1
Noweda/ NEWCHEM	Triamcinolone acetonide	1211013-02	1
Caelo	Triamcinolone acetonide	13379906	6
Caelo	Triamcinolone acetonide	13379901	1
Caelo	Triamcinolone acetonide	14355708	10
Caelo	Triamcinolone acetonide	170547902	1
Caelo	Triamcinolone acetonide	16K07-B06-333438	3
Oberlinden Apotheke	Triamcinolone acetonide	B0544/114010	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Oberlinden- Apotheke	Triamcinolone acetonide	U0544/113530	1
Oberlinden-Apotheke	Triamcinolone acetonide	U0544/1	1
Euro OTC	Triamcinolone acetonide	141201302	4
Phoenix	Triamcinolone acetonide	13126-N11	2
Phoenix	Triamcinolone acetonide	14355708	1
Phoenix	Triamcinolone acetonide	14355709	1
Phoenix	Triamcinolone acetonide	1703037	1
Phoenix	Triamcinolone acetonide	3064	1
Phoenix	Triamcinolone acetonide	1703037-01	1
Phoenix	Triamcinolone acetonide	3129	1
Phoenix	Triamcinolone acetonide	1706013-01	4
Phoenix	Triamcinolone acetonide	3219	1
Phoenix	Triamcinolone acetonide	1805001-01	1
Phoenix	Triamcinolone acetonide	18100221	1
Phoenix	Triamcinolone acetonide	3424	1
Phoenix WE 16.03.17 EK...	Triamcinolone acetonide	1612014-01	1
Caelo	Triamcinolone acetonide	15233903-20160615Ma9	1
Caelo	Triamcinolone acetonide	1903015_01	1
Phoenix_25.01.2019	Triamcinolone acetonide	1810015-01	2
phoenix-06.11.18	Triamcinolone acetonide	1801020-01	1
phönix	Triamcinolone acetonide	15430107	1
phönix	Triamcinolone acetonide	15233906	1
phönix	Triamcinolone acetonide	1605010-01	1
Phönix	Triamcinolone acetonide	12E15-N03	1
Phönix	Triamcinolone acetonide	13E15-N03	1
Phönix	Triamcinolone acetonide	13379902	1
Phönix	Triamcinolone acetonide	1403009-01	1
Phönix	Triamcinolone acetonide	13K15-B31-289027	1
Phönix	Triamcinolone acetonide	1407044-01	1
Phönix	Triamcinolone acetonide	1608005-01	1
Phönix	Triamcinolone acetonide	17057908	2
Phönix	Triamcinolone acetonide	18100204	1
Phönix	Triamcinolone acetonide	1805001-02	1
Phönix	Triamcinolone acetonide	18K16-B05-359871	2
Phönix	Triamcinolone acetonide	1903015	1
Phönix	Triamcinolone acetonide	18F14-B01-032343	1
Phönix Gotha	Triamcinolone acetonide	14355711	1
Phönix W.E: 16.04.2018 ...	Triamcinolone acetonide	1710002-01	1
Fagron	Triamcinolone acetonide	16014-B12-3231318	1
Caelo	Triamcinolone acetonide	12173705	2
Euro OTC	Triamcinolone acetonide	1612014-014	1
sanacorp	Triamcinolone acetonide	15233902	1
Sanacorp	Triamcinolone acetonide	12301506	1
Sanacorp	Triamcinolone acetonide	13124807	2
Sanacorp	Triamcinolone acetonide	13E15-N03	1
Sanacorp	Triamcinolone acetonide	1326N11	1
Sanacorp	Triamcinolone acetonide	13379905	1
Sanacorp	Triamcinolone acetonide	100/AKD4	1
Sanacorp	Triamcinolone acetonide	15430108	1
Sanacorp	Triamcinolone acetonide	17120610	1
Sanacorp	Triamcinolone acetonide	17120605	1
Sanacorp	Triamcinolone acetonide	1710002-01	1
Sanacorp	Triamcinolone acetonide	17358305	1
Sanacorp	Triamcinolone acetonide	17H03-B12-345553	1
Sanacorp	Triamcinolone acetonide	NY0485M	2
Sanacorp	Triamcinolone acetonide	18100220	1
Caelo	Triamcinolone acetonide	14355101	12
Fagron	Triamcinolone acetonide	C22H25CIN209	1
Caelo	Triamcinolone acetonide	NS0571M	1
Caelo	Triamcinolone acetonide	12E15-N03	1

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Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone acetonide	93/AD1	1
Caelo	Triamcinolone acetonide	13C13-N20	2
Caelo	Triamcinolone acetonide	95/AKD34	1
Caelo	Triamcinolone acetonide	100/AKD2	1
Fagron	Triamcinolone acetonide	13C13-N200217/412	1
Sittig	Triamcinolone acetonide	1508008-02	1
Spangro 15.1.2014	Triamcinolone acetonide	1303001-02	1
Spangro 27.03.18	Triamcinolone acetonide	17030337-01	1
VDL	Triamcinolone acetonide	13379903	1
Caelo	Triamcinolone acetonide	12173701	5
WE: 08.12.2015	Triamcinolone acetonide	14K14-B05-302887	1
	Triamcinolone acetonide	1403009-01	1
Caelo	Triamcinolone acetonide	13256607	5
Euro OTC	Triamcinolone acetonide	1303001-02	8
Euro OTC	Triamcinolone acetonide	1211013-02	9
Euro OTC	Triamcinolone acetonide		3
Euro OTC	Triamcinolone acetonide	1608005	1
Fagron	Triamcinolone acetonide	12E15-N03	21
Fagron	Triamcinolone acetonide		2
Fagron	Triamcinolone acetonide	15C19-B06-308572	6
Caelo	Triamcinolone acetonide	13379921	1

- 108 683 spectra from 742 *Apo-Ident* customers from a total of 31 369 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Triamcinolone acetonide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Triamcinolone acetonide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	582	0	110 107
Type B	0	1198	0	117 944
Type C	0	2522	42	108 683

The substance/substance group *Triamcinolone acetonide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9691 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 99.4992 %)
Type C	100.0000 % (> 99.8899 %)	98.3619 % (> 98.2449 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to

exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Triamcinolone acetonide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dexamethasone	11.63	73.07
Prednisolon dihydrogen phosphate dinat...	34.12	—
Prednisolone, micronized	34.66	86.15
Cyanocobalamin	36.41	—
Betamethasone, micronized	37.90	108.05
Sodium edetate	42.58	—
Fluocinolonacetonid, micronized	42.66	—
Erythromycin	44.55	78.91
Dexamethasone acetate	47.03	—
⋮	⋮	⋮
Betamethasone valerate	>50	51.70
Budesonide, micronized	>50	90.30
Capsaicin	>50	93.37
Prednicarbate, micronized	>50	105.06
Triamcinolone, micronized	>50	121.65
Prednisone	>50	136.44
Norethisterone acetate	>50	224.00
Heparin sodium	>50	291.75

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Triamcinolone acetonide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22313	22313	0.00	14.44
20765	20765	0.00	13.08
21072	21061	1.76	13.64
22572	22572	0.00	12.94
22752	22752	0.00	11.63
20910	21061	2.02	13.15
21587	21587	0.00	18.35
21962	21061	2.51	14.52
21061	21061	0.00	13.93
21883	21883	0.00	14.89

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Triamcinolone, micronized**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20564-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Triamcinolone, micronized; Triamcinolonum micronisatum

Special notes

When selecting the *Triamcinolone, micronized* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Triamcinolone, micronized	8	1	29

Second-stage model

For differentiation of the substance/substance group *Triamcinolone, micronized* the following second-stage model is used:

- [Submodel 1](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Triamcinolone, micronized*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Triamcinolone, m...	15106905	22273	45	20150527
Caelo	Triamcinolone, m...	15106905	22605	40	20150527
Caelo	Triamcinolone, m...	15106911	23508	40	20150527
Fagron	Triamcinolone, m...	12A03-N09	20730	40	20120117
Fagron	Triamcinolone, m...	12K07-N13	20936	80	AR-15-FG-003373-01
Fagron	Triamcinolone, m...	14B13-B30-316101	22840	40	20140311
Fagron	Triamcinolone, m...	18A19-B05-351174	24182	40	1811263
Fagron	Triamcinolone, m...	18A19-B05-351174	24182SI	32	1811263
Fagron	Triamcinolone, m...	18E09-B04-353921	24446	40	1907730
Fagron	Triamcinolone, m...	18J01-B05-364078	24944	40	2004435

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 437 spectra of 10 reference samples from the substance/substance group *Triamcinolone, micronized*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 252 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 240 spectra of 6 reference samples from the substance/substance group *Triamcinolone, micronized*.

- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Triamcinolone, micronized	17G03-B04-343670	24097	40
Fagron	Triamcinolone, micronized	17G03-B04-343670	24097SI	40
Fagron	Triamcinolone, micronized	17G03-B04-343670	24107	40
Fagron	Triamcinolone, micronized	17G03-B04-343670	24107SI	40
Fagron	Triamcinolone, micronized	18E09-B04-353921	24446SI [†]	40
Fagron	Triamcinolone, micronized	18J01-B05-364078	24944SI [†]	40

- 118 902 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 37 spectra from 30 *Apo-Ident* customers from 30 batches from the substance/substance group *Triamcinolone, micronized*.
- Among them are spectra of independent samples from 29 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Triamcinolone, micronized	12295210	1
Caelo	Triamcinolone, micronized	12295207	3
Caelo	Triamcinolone, micronized	18092104	1
Caelo	Triamcinolone, micronized	15106960	1
Caelo	Triamcinolone, micronized	13J07-N08	2
Caelo	Triamcinolone, micronized	15106902	1
Fagron	Triamcinolone, micronized	14B13-B30-316102	1
Fagron	Triamcinolone, micronized	11G26-N04	1
Fagron	Triamcinolone, micronized	11D28-N04	1
Fagron	Triamcinolone, micronized	12F01-N19	2
Fagron	Triamcinolone, micronized	13D30-N15	2
Fagron	Triamcinolone, micronized	12D02-N14	1
Fagron	Triamcinolone, micronized	13J07-N08	1
Fagron	Triamcinolone, micronized	14B13-B30-312868	1
Fagron	Triamcinolone, micronized	15B13-B30-312868	1
Fagron	Triamcinolone, micronized	NT1484M	1
Fagron	Triamcinolone, micronized	16A13-B06	1
Fagron	Triamcinolone, micronized	14B13-B30	1
Fagron	Triamcinolone, micronized	14A14-B01	1
Fagron	Triamcinolone, micronized	14B13-B30-293473	1
Fagron	Triamcinolone, micronized	12D02-N14	1
Caelo	Triamcinolone, micronized	14B13-B30-293474	1
L12	Triamcinolone, micronized	17359001	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Noweda 24.08.2015	Triamcinolone, micronized	14B13-B30-293474	1
Fagron	Triamcinolone, micronized	13C26-N04	1
Fagron	Triamcinolone, micronized	18J01-B05	1
Phönix	Triamcinolone, micronized	NS0608M	1
Sanacorp	Triamcinolone, micronized	100/AKD6	1
Sanacorp	Triamcinolone, micronized	15106916	1
Sanacorp	Triamcinolone, micronized	15106907	1
Caelo	Triamcinolone, micronized	15106912	1
Fagron	Triamcinolone, micronized	12A03-N09	1

- 111 210 spectra from 742 *Apo-Ident* customers from a total of 31 862 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Triamcinolone, micronized* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Triamcinolone, micronized* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	437	0	110 252
Type B	0	190	50	118 902
Type C	0	37	0	111 210

The substance/substance group *Triamcinolone, micronized* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.6270 %)
Type B	100.0000 % (> 99.9893 %)	79.1667 % (> 77.9167 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 83.7838 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Triamcinolone, micronized* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Prednisone	11.81	165.44
Ethinylestradiol	26.88	—
Polymyxin B sulfate	28.03	—
Cyanocobalamin	29.65	—
Methylprednisolone	31.41	—
Magnesium citrate	32.05	—
Bacitracin	32.14	—
Gramicidin	40.85	—
Minoxidil	44.02	—
Prednisolon dihydrogen phosphate dinat...	46.23	—
Ambroxol hydrochloride	46.91	—
Tyrothricin	47.34	—
Levothyroxin sodium	55.35	—
⋮	⋮	⋮
Dexamethasone	>50	44.83
Prednisolone, micronized	>50	58.34
Triamcinolone acetonide	>50	106.48
Betamethasone, micronized	>50	130.54
Erythromycin	>50	132.63
Budesonide, micronized	>50	139.09
Capsaicin	>50	145.87
Betamethasone valerate	>50	160.82
Prednicarbate, micronized	>50	182.28
Heparin sodium	>50	194.17
Norethisterone acetate	>50	446.27

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Triamcinolone, micronized* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24182	24182	0.00	12.85
24446	24446	0.00	28.30
22605	20936	7.27	57.12
23508	20936	6.85	56.95
22840	20936	8.28	52.39
22273	20936	8.43	59.20
24944	24944	0.00	26.34
20730	20936	25.60	43.00
20936	20936	0.00	54.12

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Triclosan**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20005-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Triclosan; Triclosanum

Special notes

When selecting the *Triclosan* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Triclosan	8	12	485

Second-stage model

For differentiation of the substance/substance group *Triclosan* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Triclosan*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Triclosan	13391808	21509	60	20131211
Caelo	Triclosan	14121209	21591	45	20140718
Euro OTC	Triclosan	1406032-01	21615	60	20140710
Euro OTC	Triclosan	1507041	21856	60	20150804*
Euro OTC	Triclosan	1510045	22227	60	20150511*
Euro OTC	Triclosan	1602003	22373	45	20160204*
Euro OTC	Triclosan	1701032	22987	40	20170207*
Fagron	Triclosan	17K02-B06-343548	23915	40	20180105

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 410 spectra of 8 reference samples from the substance/substance group *Triclosan*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 279 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 500 spectra of 12 reference samples from the substance/substance group *Triclosan*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Triclosan	160846	22453	60
Caelo	Triclosan	162808	22775	40
Caelo	Triclosan	171498	23315	40
Caelo	Triclosan	180814	24048	40
Caelo	Triclosan	182537	24387	40
Euro OTC	Triclosan	1607002	22674	40
Euro OTC	Triclosan	1705011	23425	40
Euro OTC	Triclosan	1708025	23699	40
Euro OTC	Triclosan	1801049	23964	40
Euro OTC	Triclosan	1901006	24466	40
Euro OTC	Triclosan	1912002	24927	40
Euro OTC	Triclosan	2001027	25097	40

- 118642 spectra from a total of 2408 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3195 spectra from 625 *Apo-Ident* customers from 519 batches from the substance/substance group *Triclosan*.
- Among them are spectra of independent samples from 478 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
30.01.2019 Phoenix	Triclosan	18081415	1
A.H.D.	Triclosan	12L06-N01	1
AEP	Triclosan	18253722	1
agron/ Noweda	Triclosan	13A11-N03	1
AHC 02.09.13 EK9,04	Triclosan	13D02-N02	1
AHD	Triclosan	17081723	1
Caelo	Triclosan	17081703	11
Caelo	Triclosan	13D02-No2	1
AHD 17.01.15	Triclosan	13L18-B35-289992	1
Caelo	Triclosan	15203606	8
Caelo	Triclosan	16280810	1
AHL	Triclosan	1801049-01	2
Caelo	Triclosan	12276827	1
ALH	Triclosan	1607002-01	2
Allianc.Healthc../Apomix	Triclosan	14F23-B02-295760	1
Caelo	Triclosan	18253705	17
Alliance Health 26.11.2...	Triclosan	13L18-B35-289995	1
Alliance Healthcare	Triclosan	12G09-N09	1
Alliance Healthcare	Triclosan	12L06-N01	1
Alliance Healthcare	Triclosan	13D02-N02	1
Alliance Healthcare	Triclosan	13L-18-835	1

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Supplier	Substance	Batch	Spectra
Alliance Healthcare	Triclosan	16084608	1
Euro OTC	Triclosan	190100601	1
Fagron	Triclosan	13H08-N-10	1
Fagron	Triclosan	13D02-N-02	1
Alliance Healthcare/Fis...	Triclosan	13H09-N01	1
Allianz	Triclosan	1801049-01	1
Anzag	Triclosan	12G09-N09	2
Anzag	Triclosan	5846205	1
Anzag	Triclosan	12G17-N04	3
Anzag	Triclosan	13L18-B35-289995	1
Anzag	Triclosan	1607002-01	2
Anzag	Triclosan	1701032-02	1
anzag 20.11.2013	Triclosan	12359114	1
Anzag 4.12.12 ek:8,89	Triclosan	12G17-N04	1
Fagron	Triclosan	13a11n03	1
Caelo	Triclosan	17081720	18
Caelo	Triclosan	12003201	3
Anzag06.	Triclosan	14F23-B02-295758	1
Apomix	Triclosan	17149813	1
Apomix/Noweda	Triclosan	1406032-01	2
Apotheke an der Bornhei...	Triclosan	16280817	3
BASF	Triclosan	1505009-01	1
BASF	Triclosan	1708025-01	1
BASF Chem trade GmbH/Ph...	Triclosan	5846205	1
BASF Grenzach GmbH/Phönix	Triclosan	13A11-N03	1
BASF Grenzach GmbH/Phönix	Triclosan	13A11-No3	1
BASF Grenzach GmbH/Phönix	Triclosan	13D02-N02	1
BASF Grenzach GmbH/Phönix	Triclosan	10006226	1
BASF Grenzach GmbH/Phönix	Triclosan	13H09-N01	1
BASF Grenzach/Noweda	Triclosan	5900346	1
Beiersdorf	Triclosan	14F23-B02-295764	1
Bionorica/Phönix	Triclosan	1708025-01	1
Bombastus	Triclosan	14f23-b02-300219	1
Bombastus	Triclosan	12359111	1
Bombastus	Triclosan	12L06-N01	2
Bombastus	Triclosan	17081726	1
Caelo	Triclosan	13A11-N03	2
Caelo	Triclosan	12359107	1
Caelo	Triclosan	3041408	1
Caelo	Triclosan	17149812	9
Caelo	Triclosan	11076716	1
Caelo	Triclosan	12003205	7
Caelo	Triclosan	11076717	2
Caelo	Triclosan	12145902	5
Caelo	Triclosan	5012E-03402	1
Caelo	Triclosan	12145906	6
Caelo	Triclosan	12145908	7
Caelo	Triclosan	12145909	10
Caelo	Triclosan	20021304	1
Caelo	Triclosan	11238011	1
Caelo	Triclosan	12145907	9
Caelo	Triclosan	12145917	1
Caelo	Triclosan	12359104	6
Caelo	Triclosan	12359110	5
Caelo	Triclosan	12359111	7
Caelo	Triclosan	13247903	1
Caelo	Triclosan	13247904	11
Caelo	Triclosan	13H08-N10	2
Caelo	Triclosan	16021306	1
Caelo	Triclosan	15121202	1

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Supplier	Substance	Batch	Spectra
Caelo	Triclosan	13391801	2
Caelo	Triclosan	13391804	9
Caelo	Triclosan	13391807	3
Caelo	Triclosan	14052102	11
Caelo	Triclosan	bhfdd	1
Caelo	Triclosan	13L18B35289993	1
Caelo	Triclosan	8081401	1
Caelo	Triclosan	13L18-B35-289995	1
Caelo	Triclosan	14121207	9
Caelo	Triclosan	14052105	1
Caelo	Triclosan	1412109	1
Caelo	Triclosan	14F23B02293859	1
Caelo	Triclosan	14211207	1
Caelo	Triclosan	14121204	8
Caelo	Triclosan	23121409	1
Caelo	Triclosan	14121210	10
Caelo	Triclosan	14121215	13
Caelo	Triclosan	14F23-B02-295760	1
Caelo	Triclosan	14205901	5
Caelo	Triclosan	150103201	1
Caelo	Triclosan	1505009	1
Caelo	Triclosan	14F23-B02-295758	1
Caelo	Triclosan	15203603	13
Caelo	Triclosan	1520603	1
Caelo	Triclosan	1501032-02	1
Caelo	Triclosan	15301501	1
Caelo	Triclosan	15C10-B06-311161	1
Caelo	Triclosan	15301504	10
Caelo	Triclosan	1503603	1
Caelo	Triclosan	1530105	1
Caelo	Triclosan	15301511	7
Caelo	Triclosan	15c10-b06	1
Caelo	Triclosan	160084601	1
Caelo	Triclosan	15G07-B03-310040	1
Caelo	Triclosan	16084602	8
Caelo	Triclosan	160846	1
Caelo	Triclosan	16084609	3
Caelo	Triclosan	16084606	4
Caelo	Triclosan	1602003-01	2
Caelo	Triclosan	16084618	13
Caelo	Triclosan	162808	1
Caelo	Triclosan	160846018	1
Caelo	Triclosan	12680801	1
Caelo	Triclosan	16084620	1
Caelo	Triclosan	16280811	13
Caelo	Triclosan	16280816	14
Caelo	Triclosan	1609005-02	2
Caelo	Triclosan	16280803	5
Caelo	Triclosan	1628082	1
Caelo	Triclosan	17081706	3
Caelo	Triclosan	16293901	1
Caelo	Triclosan	16280817	12
Caelo	Triclosan	170817075274	1
Caelo	Triclosan	17081710	16
Caelo	Triclosan	17081711	13
Caelo	Triclosan	17081709	17
Caelo	Triclosan	1609005	1
Caelo	Triclosan	170817	1
Caelo	Triclosan	16280874	1
Caelo	Triclosan	17081724	18

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Supplier	Substance	Batch	Spectra
Caelo	Triclosan	228711-514	1
Caelo	Triclosan	6121711	1
Caelo	Triclosan	17149806	6
Caelo	Triclosan	17149807	13
Caelo	Triclosan	170802501	1
Caelo	Triclosan	170817265507	1
Caelo	Triclosan	17149817	6
Caelo	Triclosan	170802-01	1
Caelo	Triclosan	1708173	1
Caelo	Triclosan	17149813	13
Caelo	Triclosan	17149824	7
Caelo	Triclosan	1714930	1
Caelo	Triclosan	1748912	1
Caelo	Triclosan	17149827	10
Caelo	Triclosan	16071801	1
Caelo	Triclosan	17149818	1
Caelo	Triclosan	17149821	25
Caelo	Triclosan	171499808	1
Caelo	Triclosan	17149822	9
Caelo	Triclosan	18081408	30
Caelo	Triclosan	1714926	1
Caelo	Triclosan	18081410	9
Caelo	Triclosan	18081415	21
Caelo	Triclosan	18253701	3
Caelo	Triclosan	1801417	1
Caelo	Triclosan	18253709	15
Caelo	Triclosan	18253715	1
Caelo	Triclosan	18253716	11
Caelo	Triclosan	18253717	4
Caelo	Triclosan	18523716	1
Caelo	Triclosan	182537001	1
Caelo	Triclosan	13391802	4
Caelo	Triclosan	18081405	24
Caelo	Triclosan	18253702	8
Caelo	Triclosan	11238003	2
Caelo	Triclosan	17801712	1
Caelo	Triclosan	11238004	1
Caelo	Triclosan	17081725	14
Caelo	Triclosan	13D02-N02	7
Caelo	Triclosan	14052103	13
Caelo	Triclosan	16280819	7
Caelo	Triclosan	17081717	4
Caelo	Triclosan	1705011-01	5
Caelo	Triclosan	17149825	16
Caelo	Triclosan	182537002	1
Caelo	Triclosan	17081716-T20180112Ma	1
Caelo	Triclosan	12359109	3
Caelo	Triclosan	17149801	5
Caelo	Triclosan	15301514	1
Caelo	Triclosan	16084611	16
Caelo	Triclosan	16280801	24
Caelo	Triclosan	18253714	3
Caelo	Triclosan	15G07-B03-310035/201	1
Caelo	Triclosan	12003202	1
Caelo	Triclosan	13L18-B35-289987	1
Caelo	Triclosan	12003210	5
Caelo	Triclosan	12359106	11
Caelo	Triclosan	17149813-T20181115Ma	1
Caelo	Triclosan	14205902	9
Caelo	Triclosan	17081723	5

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Supplier	Substance	Batch	Spectra
Caelo	Triclosan	15C10-B06-312982	3
Caelo	Triclosan	1808414	1
Caelo	Triclosan	15G07-B03-310037	2
Caelo	Triclosan	17149819	16
Caelo	Triclosan	17K02-B06_343544	2
Caelo	Triclosan	16280808	17
Caelo	Triclosan	15G07-B03-30039	1
Caelo	Triclosan	14121203	8
Caelo	Triclosan	14121214	10
Caelo	Triclosan	2317I-03402	1
Caelo	Triclosan	17149814	12
Caelo	Triclosan	1125204	1
Caelo	Triclosan	12L06-N01/0005900346	1
Caelo	Triclosan	12106-n01	1
Caelo	Triclosan	517E-03402	1
Caelo	Triclosan	17081716	12
Caelo	Triclosan	17081726	9
Caelo	Triclosan	10206240	1
Caelo	Triclosan	12145901	5
Caelo	Triclosan	17149808	27
Caelo	Triclosan	18081403	11
Caelo	Triclosan	12L06-N01	7
Caelo	Triclosan	15G07-B03-310035	1
Caelo	Triclosan	16084608	17
Caelo	Triclosan	18253718	3
Caelo	Triclosan	12G17-N04	2
Caelo	Triclosan	13L18-B35-289986	2
Caelo	Triclosan	13L18B35289986	1
Caelo	Triclosan	17149815	12
Caelo	Triclosan	17081707	22
Caelo	Triclosan	15301512	5
Caelo	Triclosan	182537052	1
Caelo	Triclosan	13247805	1
Caelo	Triclosan	1701032-01	2
Caelo	Triclosan	16280824	2
Caelo	Triclosan	12145910	11
Caelo	Triclosan	14052101	5
Caelo	Triclosan	16084607	10
Caelo	Triclosan	16064616	1
Caelo	Triclosan	16280821	2
Caelo	Triclosan	18081401	8
Caelo	Triclosan	18081406	13
Caelo	Triclosan	17149812-20180619Ma4	1
Caelo	Triclosan	14205905	5
Caelo	Triclosan	17149805	7
Caelo	Triclosan	1781720	1
Caelo	Triclosan	18081413	20
Caelo	Triclosan	18253712	8
Caelo	Triclosan	13H09-N01	7
Caelo	Triclosan	13247905	10
Caelo	Triclosan	14F23-B02-295765	1
Caelo	Triclosan	15203604	10
Caelo	Triclosan	15301502	13
Caelo	Triclosan	5203607	1
Caelo	Triclosan	15301506	16
Caelo	Triclosan	16084603	9
Caelo	Triclosan	16084617	1
Caelo	Triclosan	16280805	2
Caelo	Triclosan	160280811	1
Caelo	Triclosan	16280818	7

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Supplier	Substance	Batch	Spectra
Caelo	Triclosan	17081704	1
Caelo	Triclosan	17081713	6
Caelo	Triclosan	17081702	1
Caelo	Triclosan	1149806	1
Caelo	Triclosan	18081417	19
Caelo	Triclosan	18253711	1
Caelo	Triclosan	15301510	2
Caelo	Triclosan	12359114	1
Caelo	Triclosan	15203607	14
Caelo	Triclosan	162820817	1
Caelo	Triclosan	17081714	9
Caelo	Triclosan	17081721	18
Caelo	Triclosan	17081722	23
Caelo	Triclosan	17149809	32
Caelo	Triclosan	17149820	14
Caelo	Triclosan	18081402	10
Caelo	Triclosan	18081414	15
Caelo	Triclosan	13L18-B35-289992	2
Caelo	Triclosan	14F23-B02	1
Caelo	Triclosan	15301505	10
Caelo	Triclosan	150704101	1
Caelo	Triclosan	15C10-B06-310031	3
Caelo	Triclosan	15C10-B06-310031	1
Caelo	Triclosan	16280802	18
Caelo	Triclosan	16280809	5
Caelo	Triclosan	1714819	1
Caelo	Triclosan	18253706	16
Caelo	Triclosan	18253707	24
Caelo	Triclosan	18253/06	1
Caelo	Triclosan	18253721	7
Caelo	Triclosan	18253708	17
Caelo	Triclosan	171498085598	1
Caelo	Triclosan	12359105	7
Caelo	Triclosan	13247908	2
Caelo	Triclosan	14121220	1
Caelo	Triclosan	14121211	9
Caelo	Triclosan	14211211	1
Caelo	Triclosan	15203608	11
Caelo	Triclosan	15G07-B03-310038	2
Caelo	Triclosan	16084601	7
Caelo	Triclosan	15301513	1
Caelo	Triclosan	18081407	19
Caelo	Triclosan	18253710	1
Caelo	Triclosan	18253722	3
Caelo	Triclosan	1719814	1
Caeo/Noweda	Triclosan	15301505	1
Caeolo	Triclosan	17149809	1
Caeolo/Noweda	Triclosan	13247905	1
Caeolo/Phönix	Triclosan	18081416	1
Caesar & Loretz GmbH	Triclosan	16280811	1
Caesar & Loretz GmbH	Triclosan	1609005-01	1
Caesar & Loretz GmbH	Triclosan	17149813	1
Caesar & Loretz GmbH	Triclosan	18081403	1
Caesar & Loretz GmbH	Triclosan	17149821	1
Caesar & Loretz GmbH	Triclosan	15081416	1
Caesar & Loretz GmbH	Triclosan	18081417	1
Caesar & Loretz GmbH	Triclosan	18253706	3
Caesar & Loretz GmbH	Triclosan	18081414	1
Caesar & Loretz GmbH	Triclosan	18081410	1
Caesar & Loretz GmbH	Triclosan	18253707	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Triclosan	18253702	2
Caesar & Loretz GmbH	Triclosan	18253705	2
Caesar & Loretz GmbH	Triclosan	18253712	1
Caesar & Loretz GmbH	Triclosan	18253716	2
Caesar & Loretz GmbH	Triclosan	18253708	1
Caesar & Loretz GmbH	Triclosan	18253714	1
Caesar & Loretz GmbH	Triclosan	18253710	1
Caesar & Loretz GmbH	Triclosan	18253724	1
Caesar & Loretz GmbH	Triclosan	182537002	1
Caesar & Loretz GmbH / ...	Triclosan	18253721	1
Caesar & Loretz GmbH / ...	Triclosan	17149813	1
Caesar & Loretz GmbH / ...	Triclosan	18081413	2
Caesar & Loretz GmbH / ...	Triclosan	18081416	1
Caesar & Loretz GmbH / ...	Triclosan	18253730	1
Caesar & Loretz GmbH / ...	Triclosan	18253705	1
Caesar & Loretz GmbH, P...	Triclosan	18081417	1
Caesar & Loretz GmbH, P...	Triclosan	18253709	2
Caesar & Loretz GmbH, P...	Triclosan	18253710	1
Caesar & Loretz GmbH, P...	Triclosan	18253707	1
Caesar & Loretz GmbH/ AHD	Triclosan	18081416	1
Caesar & Loretz GmbH/Fi...	Triclosan	18081417	1
Caesar & Loretz GmbH/Go...	Triclosan	18253707	1
Caesar & Loretz GmbH/Mi...	Triclosan	18253708	1
Caesar & Loretz GmbH/Ph...	Triclosan	18253718	4
Caesar & Loretz GmbH/Ph...	Triclosan	18253712	1
Caesar & Loretz/ Noweda	Triclosan	17149812	1
Caesar & Loretz/AHC	Triclosan	16084603	2
Caesar & Loretz/AHD	Triclosan	14121209	1
Caesar u Loretz	Triclosan	15301503	1
Caesar und Loretz	Triclosan	15301502	1
Caesar&Lorenz	Triclosan	17081707	1
Caesar&Lorenz / Gehe	Triclosan	18253716	1
Caesar&Lorenz / Gehe	Triclosan	18253722	1
Caesar&Loretz GmbH	Triclosan	16084609	1
Caesar&Loretz GmbH	Triclosan	16280808	1
Caesar&Loretz GmbH/Anzag	Triclosan	14121215	2
Caesar&Loretz GmbH/Anzag	Triclosan	15203603	2
Caesar&Loretz GmbH/Sana...	Triclosan	15301505	1
Caesar&Loretz,AHC,12.12...	Triclosan	16084618	1
caesar&lorenz,Phönix	Triclosan	15203607	1
Caesar&lorenz,Phönix	Triclosan	15203606	1
Caesar/Lorenz	Triclosan	12145910	1
Caesar/Lorenz	Triclosan	12359104	1
Caesar/Lorenz	Triclosan	13247904	1
Caleo/Phönix	Triclosan	17081711	1
Cealo	Triclosan	17081723	1
Cealo	Triclosan	71215/1Gie	1
Cealo/AHD	Triclosan	14F23-B02-295947	1
Cealo/Anzag	Triclosan	182537002	1
Cealo/Gehe	Triclosan	17149807	1
DAB 2008	Triclosan	12003201	2
Delta Apotheke	Triclosan	17149822	1
E Plus	Triclosan	16280808	1
E Plus	Triclosan	17081705	1
ebe a	Triclosan	14121207	1
Eigenproduktion	Triclosan	13A11-N03	1
EuRho	Triclosan	1107030-01	2
EuRho	Triclosan	1202018-01	1
EuRho	Triclosan	1206034-02	2
EuRho	Triclosan	1408024-01	1

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Supplier	Substance	Batch	Spectra
EuRho	Triclosan	151004501	1
EuRho	Triclosan	1705011-01	1
EuRho / 30	Triclosan	1401038-01	1
EuRho / fiebig	Triclosan	1705011-01	1
EuRho/Phoenix	Triclosan	1401038-01	1
EuRho/Phönix	Triclosan	1307050-01	2
EuRhoNoweda	Triclosan	1602003-01	1
Euro OCT/Noweda	Triclosan	1501032-02	1
Euro OTC	Triclosan	CHB1303011-01	1
Euro OTC	Triclosan	160700201	1
Euro OTC	Triclosan	160900502	1
Euro OTC	Triclosan	170103202	1
Euro OTC	Triclosan	120203-02	1
Euro OTC	Triclosan	1211025-01	11
Euro OTC	Triclosan	130301101	1
Euro OTC	Triclosan	140103801	1
Euro OTC	Triclosan	1501032-01	10
Euro OTC	Triclosan	140603201	1
Euro OTC	Triclosan	700228	1
Euro OTC	Triclosan	15203607	3
Euro OTC	Triclosan	1602003-01	24
Euro OTC	Triclosan	15C10-B06-312982	1
Euro OTC	Triclosan	15G07-B03-310036	1
Euro OTC	Triclosan	160531T	1
Euro OTC	Triclosan	16047002-01	1
Euro OTC	Triclosan	12276024	1
Euro OTC	Triclosan	170113T1609005-01	1
Euro OTC	Triclosan	1701032-01	15
Euro OTC	Triclosan	170501101	2
Euro OTC	Triclosan	17081703	1
Euro OTC	Triclosan	1708025_01	1
Euro OTC	Triclosan	17149806	1
Euro OTC	Triclosan	12276028	2
Euro OTC	Triclosan	17080-01	1
Euro OTC	Triclosan	17149815	1
Euro OTC	Triclosan	1901006-02	6
Euro OTC	Triclosan	191006-02	1
Euro OTC	Triclosan	1708025-01	33
Euro OTC	Triclosan	170526T/1701032-02	1
Euro OTC	Triclosan	170511-01	1
Euro OTC	Triclosan	1408024-01	6
Euro OTC	Triclosan	4486611	2
Euro OTC	Triclosan	1107030-01	3
Euro OTC	Triclosan	1202018-01	1
Euro OTC	Triclosan	150500901	1
Euro OTC	Triclosan	1510045-01	16
Euro OTC	Triclosan	1607002-01	28
Euro OTC	Triclosan	120603402	1
Euro OTC	Triclosan	1609005-02	23
Euro OTC	Triclosan	1901006-03	2
Euro OTC	Triclosan	5860088	1
Euro OTC	Triclosan	1705011-01	34
Euro OTC	Triclosan	18253706	2
Euro OTC	Triclosan	1505009-01	12
Euro OTC	Triclosan	1206034-01	1
Euro OTC	Triclosan	14F23-B02-295948	1
Euro OTC	Triclosan	1507041-01	6
Euro OTC	Triclosan	12276023	1
Euro OTC	Triclosan	16084614	1
Euro OTC	Triclosan	171121T/1705011-01	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Triclosan	160702-01	1
Euro OTC	Triclosan	1303011-01	5
Euro OTC	Triclosan	190100602	1
Euro OTC	Triclosan	15G07-B03-310040	1
Euro OTC	Triclosan	170825-01	1
Euro OTC	Triclosan	180149-01	1
Euro OTC	Triclosan	169005-02	1
Euro OTC	Triclosan	15150229	2
Euro OTC	Triclosan	1701032_01	1
Euro OTC	Triclosan	17149812	1
Euro OTC	Triclosan	151004501	1
Euro OTC	Triclosan	1801049-21	1
Euro OTC	Triclosan	1206034-02	3
Euro OTC	Triclosan	1307050-01	6
Euro OTC	Triclosan	1245	1
Euro OTC	Triclosan	1901006-01	18
Euro UTC	Triclosan	1510045-01	1
Euro/Anzag	Triclosan	1607002-01	1
Euro/Gehe	Triclosan	1602003-01	1
Euro/Noweda	Triclosan	1607002-01	1
Euro/Phönix	Triclosan	170103201	1
Euro/Phönix	Triclosan	160900502	1
Euro/Phönix	Triclosan	1901006	2
Euroct/Gehe	Triclosan	1510045-01	2
Euroo/direkt	Triclosan	1705011-01	1
Euro OTC	Triclosan	15C10-B06-312981	1
Euro OTC	Triclosan	1701032-02	13
Euro OTC	Triclosan	1501032-02	4
Euro OTC	Triclosan	13H08-N10	1
Euro OTC	Triclosan	17081722	1
Euro OTC	Triclosan	15058946	2
Euro OTC	Triclosan	1401038-01	10
Euro OTC	Triclosan	1202018-02	2
Euro OTC	Triclosan	1801049-01	9
Euro OTC	Triclosan	170132-01	1
Euro OTC	Triclosan	1609005-01	28
Euro OTC	Triclosan	17K02-B06-343548	2
Euro OTC	Triclosan	160200301	1
Euro OTC	Triclosan	170802501	1
Europ Ots Pharma	Triclosan	13D02-N02	1
Fagro/Gehe	Triclosan	13H08-N10	1
Fagro/Sanacorp	Triclosan	TCS0214037	1
Fagron	Triclosan	90000383	1
Fagron	Triclosan	6012014E	1
Fagron	Triclosan	15C10-B06-310032	4
Fagron	Triclosan	15C10-B06-312981	24
Fagron	Triclosan	17K02-B06-343543	1
Fagron	Triclosan	11H09-N02	6
Fagron	Triclosan	11h09-n02	1
Fagron	Triclosan	12C21-N05	23
Fagron	Triclosan	11J28-n02	1
Fagron	Triclosan	12G09-N09	5
Fagron	Triclosan	1209213402	1
Fagron	Triclosan	12G17-N04	30
Fagron	Triclosan	11c21-n05	1
Fagron	Triclosan	2901313402	1
Fagron	Triclosan	11A05-N13	1
Fagron	Triclosan	12G17N04	1
Fagron	Triclosan	13A11-N03	10
Fagron	Triclosan	12L06-n01	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triclosan	13A11N03	1
Fagron	Triclosan	13D02-N02	65
Fagron	Triclosan	12106-n01	1
Fagron	Triclosan	2513Q-03402	1
Fagron	Triclosan	13D02N02	1
Fagron	Triclosan	13092012C	1
Fagron	Triclosan	13d02-n02	1
Fagron	Triclosan	13H08-N10	30
Fagron	Triclosan	13H08N10	2
Fagron	Triclosan	1006226	1
Fagron	Triclosan	9000383	2
Fagron	Triclosan	14022014C	1
Fagron	Triclosan	13h09-n01	1
Fagron	Triclosan	13L18-B35-289988	1
Fagron	Triclosan	13L18-B35-289986	5
Fagron	Triclosan	13L18B35289987	1
Fagron	Triclosan	13L18-B35-289983	10
Fagron	Triclosan	13L18-B35-289985	12
Fagron	Triclosan	13118-b35-289984	1
Fagron	Triclosan	13L18-B35-289987	6
Fagron	Triclosan	2914E-03402	1
Fagron	Triclosan	18082014B	1
Fagron	Triclosan	13L18-B35-289993	4
Fagron	Triclosan	13L18-B35-289995	7
Fagron	Triclosan	13H09N01	2
Fagron	Triclosan	13L18-B35-289985	1
Fagron	Triclosan	13L18-B35-289994	7
Fagron	Triclosan	13L18-B35_289995	1
Fagron	Triclosan	13L18-B35-289992	2
Fagron	Triclosan	106666066	1
Fagron	Triclosan	10112014C	1
Fagron	Triclosan	14F23-B02-293852	2
Fagron	Triclosan	14F23-B02-295765	5
Fagron	Triclosan	14F-B02-293859	1
Fagron	Triclosan	14F23-B02-295763	3
Fagron	Triclosan	14F23B02295763	1
Fagron	Triclosan	13118-b35-289994	1
Fagron	Triclosan	190615A	1
Fagron	Triclosan	14f23-b02-295758	3
Fagron	Triclosan	14F23-B02-295758	11
Fagron	Triclosan	14F23B02300219	1
Fagron	Triclosan	15G07-B03-310037	13
Fagron	Triclosan	15G07-B03-310041	1
Fagron	Triclosan	15G07-B03-30037	1
Fagron	Triclosan	15G07B03310037	1
Fagron	Triclosan	15G01-B03-310038	1
Fagron	Triclosan	15C10-B06-311161	11
Fagron	Triclosan	15C10B06311161	2
Fagron	Triclosan	15c10-B06-311161	1
Fagron	Triclosan	15C10-B06-312982	14
Fagron	Triclosan	15C10-B06	5
Fagron	Triclosan	15c10-b06-312980	1
Fagron	Triclosan	15G07	1
Fagron	Triclosan	15C10B06312982	1
Fagron	Triclosan	15C10B06312983	1
Fagron	Triclosan	15C10-B06-312980	5
Fagron	Triclosan	15g07-b03-310035	1
Fagron	Triclosan	151010-B06-312984	1
Fagron	Triclosan	15C10-806-312981	1
Fagron	Triclosan	K001-1/14/12/823	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triclosan	1708025-01	1
Fagron	Triclosan	17149817	2
Fagron	Triclosan	17148812	1
Fagron	Triclosan	17K02-B06-343547	3
Fagron	Triclosan	14F23-Bo2-295947	1
Fagron	Triclosan	17K02-B06-343544	2
Fagron	Triclosan	15G07-B03-310038	6
Fagron	Triclosan	10J18-N01	2
Fagron	Triclosan	14F23-B02-295947	4
Fagron	Triclosan	15G07-B03-310035	8
Fagron	Triclosan	17K02-B06-343546	2
Fagron	Triclosan	434083	1
Fagron	Triclosan	12L06-N01	33
Fagron	Triclosan	14F23-B02-295760	10
Fagron	Triclosan	14F23-B02-295759	9
Fagron	Triclosan	15c10-B06-312980	1
Fagron	Triclosan	TCS0214037	2
Fagron	Triclosan	13D02-N02	1
Fagron	Triclosan	11L19-N11	7
Fagron	Triclosan	13H09-No1	1
Fagron	Triclosan	11J28-N02	4
Fagron	Triclosan	15G07B03310040	1
Fagron	Triclosan	12G17-n04	2
Fagron	Triclosan	18253706	2
Fagron	Triclosan	13L18-B35-289984	4
Fagron	Triclosan	14f23-b02-295757	1
Fagron	Triclosan	15203604	1
Fagron	Triclosan	17K02-B06	7
Fagron	Triclosan	16084614	1
Fagron	Triclosan	12c21-n05	3
Fagron	Triclosan	15G047-B03-0001	1
Fagron	Triclosan	16084603	1
Fagron	Triclosan	5846205	2
Fagron	Triclosan	13Do2-N02	1
Fagron	Triclosan	10006226	2
Fagron	Triclosan	15C10-B06-310031	5
Fagron	Triclosan	17149815	1
Fagron	Triclosan	14F23-B02-295761	11
Fagron	Triclosan	13L18-B35-289	1
Fagron	Triclosan	160614	1
Fagron	Triclosan	700228-0005	1
Fagron	Triclosan	14F23-B02-295762	3
Fagron	Triclosan	200315B	1
Fagron	Triclosan	14F23-B02-295756	2
Fagron	Triclosan	15C10-B06-312983	7
Fagron	Triclosan	17081702	1
Fagron	Triclosan	13h08-n10	1
Fagron	Triclosan	13H08-N100450/1231	1
Fagron	Triclosan	13H09-N01	58
Fagron	Triclosan	15C-B06-312982	1
Fagron	Triclosan	13d02-N02	1
Fagron	Triclosan	13L18-B35	12
Fagron	Triclosan	13L-18-B35-289985	1
Fagron	Triclosan	14F23-B02-295764	2
Fagron	Triclosan	14F23-B02	5
Fagron	Triclosan	14F23-B02_295756	1
Fagron	Triclosan	11777748	4
Fagron	Triclosan	14F23-B02-300219	7
Fagron	Triclosan	15G07-B03-310036	3
Fagron	Triclosan	17G07-B03-310038	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triclosan	15C10-B06_312980	1
Fagron	Triclosan	4394083	1
Fagron	Triclosan	1214I03402	1
Fagron	Triclosan	13L18-35-289995	1
Fagron	Triclosan	15G07-B03-310040	5
Fagron	Triclosan	10666066	2
Fagron	Triclosan	15G07-B03-310039	3
Fagron	Triclosan	14F23-B02-2959947	1
Fagron	Triclosan	15C10-B06-3161	1
Fagron	Triclosan	15301510	1
Fagron	Triclosan	15c10-B06-312981	1
Fagron	Triclosan	15c10-b06-312981	1
Fagron	Triclosan	12g17-n04	2
Fagron	Triclosan	14F23-B02-295757	5
Fagron	Triclosan	15G07-B03	3
fargon	Triclosan	12G17-N04	1
Fargon	Triclosan	4394403	1
Fargon	Triclosan	12C21-N05	1
Fargon	Triclosan	13D02-N02	2
Fargon	Triclosan	14F23-B02-295948	1
Faron	Triclosan	14F23-B02-300219	2
Fiebig	Triclosan	15C10-B06-312923	1
Fiebig	Triclosan	1607002-01	1
Fiebig	Triclosan	16280811	1
Fiebig	Triclosan	17149819	1
Fiebig	Triclosan	17149814	1
Fiebig	Triclosan	17149813	1
Fiebig	Triclosan	17149821	1
Fiebig	Triclosan	18081413	2
Fischar/Gehe	Triclosan	13D02-N02	1
Fragron	Triclosan	13D02-N02	1
Fragron	Triclosan	15G07-B03-310040	1
Gehe	Triclosan	11J28-N02	1
Gehe	Triclosan	12145910	1
Gehe	Triclosan	12106-n01	1
Gehe	Triclosan	13A11-N03	1
Gehe	Triclosan	12359105	1
Gehe	Triclosan	12359104	1
Gehe	Triclosan	13D02-N02	1
Gehe	Triclosan	12359112	1
Gehe	Triclosan	12359114	1
Gehe	Triclosan	13391804	2
Gehe	Triclosan	13391811	1
Gehe	Triclosan	14052105	1
Gehe	Triclosan	1408024-01	2
Gehe	Triclosan	14121210	1
Gehe	Triclosan	14121211	1
Gehe	Triclosan	14205904	1
Gehe	Triclosan	1505009-01	1
Gehe	Triclosan	16084614	1
Gehe	Triclosan	16280801	2
Gehe	Triclosan	16280811	1
Gehe	Triclosan	16280808	1
Gehe	Triclosan	1701032-01	1
Gehe	Triclosan	1705011-01	1
Gehe	Triclosan	1701032-02	1
Gehe	Triclosan	17149816	1
Gehe	Triclosan	17149806	1
Gehe	Triclosan	1901006-01	2
Gehe	Triclosan	18253716	1

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continued from previous page

Supplier	Substance	Batch	Spectra
GEHE	Triclosan	1701032-01	1
GEHE	Triclosan	17081710	1
GEHE	Triclosan	1701032-02	1
GEHE	Triclosan	17149824	1
GEHE	Triclosan	18253724	1
Caelo	Triclosan	13L18-B35-289984	1
Caelo	Triclosan	11777748	3
GEHE 17.06.2014	Triclosan	14052102	1
GEHE 22.04.2014	Triclosan	13391804	1
Caelo	Triclosan	14205904	6
Caelo	Triclosan	15301503	10
Caelo	Triclosan	18081416	13
Euro OTC	Triclosan	14121204	1
Fagron	Triclosan	17149814	3
Fagron	Triclosan	13L18B35289984	1
Gehe/Fragon	Triclosan	15C10B06312981	2
Fagron	Triclosan	14F23-B02295757	1
Gehe-Fragon	Triclosan	15G07B03310036	2
Gehe-Fragon	Triclosan	14F23B02300219	2
Caelo	Triclosan	16084610	9
Gutenberg-Apotheke	Triclosan	13H09-N01	2
Gutenberg-Apotheke	Triclosan	13L18-B35	1
Henry Lamotte/ Noweda	Triclosan	15203606	1
Ichthyol Gesellschaft//...	Triclosan	1701032-02	1
Jenne	Triclosan	18081417	3
Klosterring	Triclosan	18081405	1
Kremer/Phönix	Triclosan	15/157/T	1
Krieger	Triclosan	12g17-N04	1
Fagron	Triclosan	15607-B03-310035	1
Kumar Organic/Noweda	Triclosan	15C10-B06	1
L12	Triclosan	16280819	1
L12	Triclosan	1628081917181722	1
L12	Triclosan	18081408	1
Caelo	Triclosan	170501101	1
L30/Alliance	Triclosan	1607002-01	1
Midas	Triclosan	17081714	2
Midas	Triclosan	17081721	1
Midas	Triclosan	17149819	1
Midas	Triclosan	17149815	1
Mvda_ 23.01.2019	Triclosan	18081416	1
Noweda	Triclosan	18253707	1
Nowed 18.12.2014	Triclosan	14121210	2
noweda	Triclosan	13L18-B35-289985	1
Noweda	Triclosan	12359107	1
Noweda	Triclosan	12G17-N04	2
Noweda	Triclosan	13247903	1
Noweda	Triclosan	14F23-B02-295765	1
Noweda	Triclosan	15203603	2
Noweda	Triclosan	15203604	1
Noweda	Triclosan	1408024-01	1
Noweda	Triclosan	16280818	1
Noweda	Triclosan	17081703	1
Noweda	Triclosan	17081711	1
Noweda	Triclosan	17149801	1
Noweda	Triclosan	1705011-01	1
Noweda	Triclosan	18253705	1
Noweda	Triclosan	18253708	1
Noweda 06.12.2019	Triclosan	18253721	1
Bombastus	Triclosan	13L18-35-289984	1
Caelo	Triclosan	17081705	9

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Noweda/EuRo	Triclosan	1801049-01	1
Fagron	Triclosan	13H09-N011296/2856	1
Fagron	Triclosan	14F23-B02-295948	4
Fagron	Triclosan	14F23B02295758	1
Fagron	Triclosan	15C10B06310031	2
Euro OTC	Triclosan	1801049	1
Caelo	Triclosan	18253726	1
phoenix	Triclosan	17081707	2
Phoenix	Triclosan	12003202	1
Phoenix	Triclosan	14205903	1
Phoenix	Triclosan	15C10-B06	1
Phoenix	Triclosan	16084614	1
Phoenix	Triclosan	1701032-01	1
Phoenix	Triclosan	16280809	2
Phoenix	Triclosan	1701032-02	1
Phoenix	Triclosan	1609005-02	1
Phoenix	Triclosan	17081721	1
Phoenix	Triclosan	17081723	2
Phoenix	Triclosan	17149809	1
Phoenix	Triclosan	17K02-B06-343547	1
Phoenix	Triclosan	17149820	1
Phoenix	Triclosan	18081408	1
Phoenix	Triclosan	18081414	1
Phoenix	Triclosan	18253706	1
Phoenix	Triclosan	18253708	1
Phoenix	Triclosan	18253705	1
Phoenix	Triclosan	18081407	1
Phoenix	Triclosan	18253716	2
Phoenix	Triclosan	1901006-01	1
Phoenix	Triclosan	3417	1
Phoenix	Triclosan	18253721	3
Phoenix	Triclosan	18253717	1
Phoenix	Triclosan	18253718	1
Phoenix 19.11.14	Triclosan	14121207	1
Caelo	Triclosan	12359108	13
Caelo	Triclosan	16253716	1
Phonix	Triclosan	13L18-B35	1
phönix	Triclosan	17081712	1
Phönix	Triclosan	12145908	1
Phönix	Triclosan	12L06-N01	1
Phönix	Triclosan	12359111	1
Phönix	Triclosan	12359109	1
Phönix	Triclosan	13A11-N03	1
Phönix	Triclosan	13H09-N01	1
Phönix	Triclosan	13L18-B35-289995	2
Phönix	Triclosan	13L18-B35-289985	1
Phönix	Triclosan	13L8-B35	1
Phönix	Triclosan	1516A-03402	1
Phönix	Triclosan	16280801	1
Phönix	Triclosan	16280811	2
Phönix	Triclosan	17081725	1
Phönix	Triclosan	3180	1
Phönix	Triclosan	18081415	1
Phönix 27.6.2019	Triclosan	18253705	1
Phönix 5.4.19	Triclosan	18253706	2
Phönix Berlin / Lamotte	Triclosan	17081711	1
Caelo	Triclosan	12359112	8
Phönix Gotha	Triclosan	13391807	1
Phönix Gotha	Triclosan	1408024-01	2
Phönix Mvda 3.7.2019	Triclosan	18253714	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Triclosan	14205903	11
Caelo	Triclosan	16084614	15
Caelo	Triclosan	17081712	13
Euro OTC	Triclosan	160900-02	1
Euro OTC	Triclosan	1550229	1
Raben-Apotheke Mildenau	Triclosan	13L18-B35-289984	2
Rondell Apotheke	Triclosan	11965460	1
Sana 06.11.14 EK 3,38	Triclosan	14121209	1
sana corp	Triclosan	12359106	1
sanacorp	Triclosan	13L18-B35-289987	1
Sanacorp	Triclosan	12359105	2
Sanacorp	Triclosan	12359106	1
Sanacorp	Triclosan	13D02-N02	1
Sanacorp	Triclosan	13247904	2
Sanacorp	Triclosan	13391807	2
Sanacorp	Triclosan	26/AKD1	1
Sanacorp	Triclosan	14052103	1
Sanacorp	Triclosan	14121211	1
Sanacorp	Triclosan	28/AKD4	1
Sanacorp	Triclosan	14121215	1
Sanacorp	Triclosan	1505009-01	1
Sanacorp	Triclosan	151004501	1
Sanacorp	Triclosan	17081725	1
Sanacorp	Triclosan	17149806	1
Sanacorp	Triclosan	17149812	1
Sanacorp	Triclosan	17149808	1
Sanacorp	Triclosan	17149814	1
Sanacorp	Triclosan	18081415	1
Sanacorp	Triclosan	18253702	1
Caelo	Triclosan	1507041-01	2
Caelo	Triclosan	1607002-01	2
Sanacorp WE: 30.04.18 E...	Triclosan	1708025-01	1
Sanacorp WE:05.09.16 ...	Triclosan	1602003-01	2
Caelo	Triclosan	12c21-n05	1
Fagron	Triclosan	C12H7C1302	1
Caelo	Triclosan	11238009	2
Caelo	Triclosan	AKD12	1
Fagron	Triclosan	11238004	1
Sonnenberg-Apotheke	Triclosan	13L18-B35-289995	1
Fagron	Triclosan	13A11-N03	1
Spangropharm	Triclosan	13D02-V02	1
Caelo	Triclosan	16280820	11
Fagron	Triclosan	11D20-N10	1
Fagron	Triclosan	12G09-no9	1
triclosan	Triclosan	15C10-B06-310032	1
WE:02.04.2016 Sanacorp ...	Triclosan	15C10-B06-312982	3
18253716	Triclosan		1
Fagron	Triclosan		5
Audor Pharma	Triclosan		2
Caelo	Triclosan	13391808	9
Caelo	Triclosan	14121209	6
Caelo	Triclosan		1
Euro OTC	Triclosan	1406032-01	10
Euro OTC	Triclosan	1602003	1
Euro OTC	Triclosan	1701032	1
Euro OTC	Triclosan		1
EurRho/Gehe	Triclosan		1
Fagron	Triclosan	17K02-B06-343548	1
Phönix	Triclosan		1
Sanacorp	Triclosan		1

- 108 052 spectra from 741 *Apo-Ident* customers from a total of 31 378 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Triclosan* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Triclosan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	410	0	110 279
Type B	0	500	0	118 642
Type C	0	3146	49	108 052

The substance/substance group *Triclosan* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5366 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.8000 %)
Type C	100.0000 % (> 99.8899 %)	98.4664 % (> 98.3725 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Triclosan* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sodium cromoglicate	24.70	—
Oxytetracycline hydrochloride	33.61	—
Chloramphenicol	48.22	—
Levothyroxin sodium	54.71	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Triclosan* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21509	22373	2.98	41.54
21591	22373	3.40	42.41
21615	22373	4.59	41.96
21856	21856	0.00	42.67
22227	22227	0.00	44.07
22373	22373	0.00	41.27
22987	22987	0.00	44.79
23915	22987	7.20	44.20

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Trometamol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20004-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Trometamol; Trometamolum

Special notes

When selecting the *Trometamol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Trometamol	6	2	143

Second-stage model

For differentiation of the substance/substance group *Trometamol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Trometamol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Trometamol	14050002	21358	40	20140220
Caelo	Trometamol	161688	22629	40	20160615*
Caelo	Trometamol	16168810	23498	40	20160615
Euro OTC	Trometamol	1803016	24063	40	20180320*
Fagron	Trometamol	13E22-N05	20856	40	AR-17-FG-016395-01
Fagron	Trometamol	18A23-B10-351258	24816	40	20180306

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 6 reference samples from the substance/substance group *Trometamol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 449 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Trometamol*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Trometamol	173208	23787	40
Fagron	Trometamol	17A16-B04-334121	23516	40
Fagron	Trometamol	17A16-B04-334121	23517	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 709 spectra from 362 *Apo-Ident* customers from 150 batches from the substance/substance group *Trometamol*.
- Among them are spectra of independent samples from 142 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
AHD	Trometamol	13095910	1
AHD	Trometamol	17320801	1
Anzag	Trometamol	12113512	1
Anzag	Trometamol	13095911	1
ANZAG	Trometamol	12113512	1
Fagron	Trometamol	10B26-N05	1
Caelo	Trometamol	11376006	8
Bombastus	Trometamol	17320811	1
Bombastus	Trometamol	18197103	1
Caelo	Trometamol	15377605	1
Caelo	Trometamol	16168820	19
Caelo	Trometamol	11160706	1
Caelo	Trometamol	11376005	5
Caelo	Trometamol	11160707	1
Caelo	Trometamol	26111201	1
Caelo	Trometamol	11160714	2
Caelo	Trometamol	213E-02519	1
Caelo	Trometamol	1001312519	1
Caelo	Trometamol	12113502	3
Caelo	Trometamol	12113505	1
Caelo	Trometamol	12113512	10
Caelo	Trometamol	13095901	10
Caelo	Trometamol	12113515	4
Caelo	Trometamol	12113510	2
Caelo	Trometamol	11160711	1
Caelo	Trometamol	21082013A	1
Caelo	Trometamol	13095910	5
Caelo	Trometamol	13095905	1
Caelo	Trometamol	27111304	1
Caelo	Trometamol	8031301	1
Caelo	Trometamol	13095915	4
Caelo	Trometamol	13339103	7
Caelo	Trometamol	13051401	1
Caelo	Trometamol	14050003	2
Caelo	Trometamol	14332402	23

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Supplier	Substance	Batch	Spectra
Caelo	Trometamol	23062015B	1
Caelo	Trometamol	18081503	1
Caelo	Trometamol	8721	1
Caelo	Trometamol	150703	1
Caelo	Trometamol	15070309	1
Caelo	Trometamol	15277602	1
Caelo	Trometamol	15377607	30
Caelo	Trometamol	161013T/15377607	1
Caelo	Trometamol	15377611	22
Caelo	Trometamol	16168807	1
Caelo	Trometamol	171978	1
Caelo	Trometamol	18041815	1
Caelo	Trometamol	17197806	2
Caelo	Trometamol	18197101	4
Caelo	Trometamol	18197109	4
Caelo	Trometamol	17320611	1
Caelo	Trometamol	13095911	12
Caelo	Trometamol	15070308	27
Caelo	Trometamol	12113507	3
Caelo	Trometamol	13095913	3
Caelo	Trometamol	14050006	1
Caelo	Trometamol	14332404	1
Caelo	Trometamol	15094404	1
Caelo	Trometamol	4616M-02519	1
Caelo	Trometamol	17320816	16
Caelo	Trometamol	13C-08-N07	1
Caelo	Trometamol	16D14-b-09-328729	1
Caelo	Trometamol	12113506	8
Caelo	Trometamol	18197103	8
Caelo	Trometamol	13095902	10
Caelo	Trometamol	17320811	28
Caelo	Trometamol	14050004	3
Caelo	Trometamol	15377602	22
Caelo	Trometamol	15377604	2
Caelo	Trometamol	3308	1
Caelo	Trometamol	3713E-02519	1
Caelo	Trometamol	16168812	2
Caelo	Trometamol	16168801	1
Caelo	Trometamol	5012M-02519	1
Caelo	Trometamol	13339107	8
Caelo	Trometamol	914I-02519	1
Caelo	Trometamol	215I-02519	1
Caelo	Trometamol	5315I-02519	1
Caelo	Trometamol	17197804	16
Caelo	Trometamol	16168825	1
Caelo	Trometamol	13339108	11
Caelo	Trometamol	15070311	21
Caelo	Trometamol	1180116	1
Caelo	Trometamol	16168819	16
Caelo	Trometamol	1339103	1
Caelo	Trometamol	13095912	14
Caelo	Trometamol	15070307	4
Caelo	Trometamol	15070304	10
Caelo	Trometamol	1618810	1
Caelo	Trometamol	17053184	1
Caelo	Trometamol	181016182	1
Caelo	Trometamol	17197809	6
Caelo	Trometamol	3439	1
Caelo	Trometamol	314Q2519	1
Caelo	Trometamol	14332403	1

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Supplier	Substance	Batch	Spectra
Caelo	Trometamol	17320804	22
Caelo	Trometamol	19088705	1
Caelo	Trometamol	16168816	2
Caelo	Trometamol	17020304	10
Caelo	Trometamol	17320801	29
Caelo	Trometamol	1730804	1
Caelo	Trometamol	15094401	14
Caelo	Trometamol	17320810	1
Caesar & Loretz GmbH	Trometamol	14050003	1
Caesar & Loretz GmbH	Trometamol	17320811	1
Caesar & Loretz GmbH	Trometamol	18197101	2
Caesar & Loretz GmbH	Trometamol	19088705	1
Caesar & Loretz GmbH / ...	Trometamol	19088705	1
Caesar & Loretz GmbH, 4...	Trometamol	11160714	1
Caesar & Loretz GmbH, 4...	Trometamol	13095902	1
Caesar & Loretz GmbH/ AHD	Trometamol	18197108	1
Caesar&Loretz	Trometamol	16168820	1
Celo/Phönix	Trometamol	16168810	1
Euro OTC	Trometamol	17197809	1
Euro OTC	Trometamol	17320804	1
Euro OTC	Trometamol	18197101	1
Fagron	Trometamol	17A16-B04	1
Fagron	Trometamol	294101	1
Fagron	Trometamol	12k14no5	1
Fagron	Trometamol	12I27-N03	1
Fagron	Trometamol	13/19-B02-286158	3
Fagron	Trometamol	13119-B02	1
Fagron	Trometamol	14F19-B03-304293	4
Fagron	Trometamol	14F19-B03	1
Fagron	Trometamol	16D14-B09	1
Fagron	Trometamol	16D14-B09-328729	2
Fagron	Trometamol	17A16-B04-340796	1
Fagron	Trometamol	16(18A23-B10-347884	1
Fagron	Trometamol	12I27-No3	1
Fagron	Trometamol	12K14-N05	2
Fagron	Trometamol	13C08-N07	3
Fagron	Trometamol	13/19-B02-293595	2
Fagron	Trometamol	8386H037	1
Fagron	Trometamol	13/19-B02	1
Fagron	Trometamol	13119-B02-286158	1
Fagron	Trometamol	610I-02519	1
Fagron	Trometamol	8386E050	1
Fagron	Trometamol	12E25-B40	1
Fagron	Trometamol	16d14-b09-328729	1
Fagron	Trometamol	17A16-B04-345550	1
Fagron	Trometamol	18A23-B10-349673	1
Fagron	Trometamol	13I19-B02-293595	1
Fagron	Trometamol	17320816	1
Fagron	Trometamol	13I19-B02	1
Fagron	Trometamol	13I19-B02-286158	1
Fargon/Kehr	Trometamol	17A16-B04-337589	1
Fiebig	Trometamol	16168825	1
Fiebig	Trometamol	17320804	1
Gatt-Koller	Trometamol	1801776	1
Gatt-Koller	Trometamol	1804167	1
Gehe	Trometamol	11160708	1
Gehe	Trometamol	11025103	1
Gehe	Trometamol	13E22-N05	1
Gehe	Trometamol	15377611	1
Gehe	Trometamol	18197101	1

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Supplier	Substance	Batch	Spectra
GEHE	Trometamol	16168810	1
GEHE	Trometamol	18A23-B10	1
Fagron	Trometamol	17A16-B04-334121	3
Caelo	Trometamol	17320801/1160518	1
Gehe/Fragron	Trometamol	18A23-B10	1
Jenne	Trometamol	17320811	1
Klenk	Trometamol	13095902	2
Krieger am 17.08.2018	Trometamol	17320801	1
Merck	Trometamol	8386F017	1
Midas	Trometamol	17197804	1
Noweda	Trometamol	11376005	1
Phoenix	Trometamol	16168819	1
Phoenix	Trometamol	3039	1
Phoenix	Trometamol	3114	1
Phoenix	Trometamol	17197804	1
Phoenix	Trometamol	3218	1
Phoenix	Trometamol	18197109	1
Phoenix	Trometamol	3409	1
Caelo	Trometamol	12113511	1
Phoenix/Cealo	Trometamol	16168825	1
Phönix	Trometamol	12113512	1
Phönix	Trometamol	13095912	2
Phönix	Trometamol	14332402	1
Phönix	Trometamol	16168819	1
Phönix	Trometamol	17197804	1
Phönix	Trometamol	17320804	1
Phönix	Trometamol	17320816	1
Caelo	Trometamol	19197103	1
Phönix Gotha	Trometamol	1319-B02-286158	1
Phönix Gotha	Trometamol	13/19-B02-286158	1
Sanacorp	Trometamol	12113506	1
Sanacorp	Trometamol	13095912	1
Sanacorp	Trometamol	3686G018	1
Sanacorp	Trometamol	15377602	1
Sanacorp	Trometamol	8386H037	1
Sanacorp	Trometamol	16168820	1
Sanacorp	Trometamol	17320804	1
Euro OTC	Trometamol	1203005-02	3
Sanocorp WE:21.05.16 EK...	Trometamol	15070311	2
Spangro 25.02.2019	Trometamol	18197101	1
Caelo	Trometamol	14050002	7
Caelo	Trometamol		4
Caelo	Trometamol	16168810	32
Fagron	Trometamol	13E22-N05	5
Fagron	Trometamol	18A23-B10-351258	1

- 110 538 spectra from 742 *Apo-Ident* customers from a total of 31 742 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Trometamol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Trometamol* and it was evaluated

how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	120	0	119 022
Type C	0	706	3	110 538

The substance/substance group *Trometamol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.5769 % (> 99.1537 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Trometamol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Aciclovir	27.68	—
Arginine	36.81	—
Menthol	43.97	—
Uridine	46.97	—
Carmellose sodium (400 / 450 / 500 / 6...	47.14	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Trometamol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20856	20856	0.00	32.40
21358	24063	3.56	40.29
22629	22629	0.00	37.85
23498	22629	6.32	36.82
24063	24063	0.00	37.46
24816	22629	5.33	35.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tropicamide**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20598-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tropicamide; Tropicamidum

Special notes

When selecting the *Tropicamide* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tropicamide	3	2	18

Second-stage model

For differentiation of the substance/substance group *Tropicamide* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tropicamide*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Tropicamide	14D23-B04-293294	21685	60	AR-15-FG-001641-01
Fagron	Tropicamide	16G19-B05-324829	22885	40	20160905
Fagron	Tropicamide	17J06-B04-341322	23982	40	1807428

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Tropicamide*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Tropicamide*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Audor Pharma	Tropicamide	APFP/TD003/09/17/TR	23983	40
Fagron	Tropicamide	17D25-B07-336833	23506	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 28 spectra from 11 *Apo-Ident* customers from 19 batches from the substance/substance group *Tropicamide*.
- Among them are spectra of independent samples from 18 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ALH	Tropicamide	15F18-B04-310971	1
Caelo	Tropicamide	17J06-B04-348766	1
Fagron	Tropicamide	12F18-N06	4
Fagron	Tropicamide	20021302	1
Fagron	Tropicamide	14D23B04293294	1
Fagron	Tropicamide	23071508	1
Fagron	Tropicamide	14104-b02-315694	1
Fagron	Tropicamide	15F18-B04-308977	1
Fagron	Tropicamide	FP/TD/003/09/17	1
Fagron	Tropicamide	18H14-B06-357220	1
Fagron	Tropicamide	18H14-B06-362476	1
Fagron	Tropicamide	17J06-B04-341323	1
Fagron	Tropicamide	12104-n03	1
Gehe	Tropicamide	15F-18B-04	1
Gehe	Tropicamide	15F18-B04	1
GEHE	Tropicamide	18H14-B06	2
Phoenix	Tropicamide	14L04-B02	2
PHÖNIX	Tropicamide	16G19-B05-324829	1
PHÖNIX	Tropicamide	17J06-B04	5

- 111 219 spectra from 742 *Apo-Ident* customers from a total of 31 872 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tropicamide* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tropicamide* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110 549
Type B	0	80	0	119 062
Type C	0	28	0	111 219

The substance/substance group *Tropicamide* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 78.5714 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tropicamide* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
L-carnitine tartrate	53.32	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tropicamide* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21685	21685	0.00	36.59
22885	23982	6.64	38.87
23982	23982	0.00	39.31

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tyrosine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21574-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tyrosine; Tyrosinum

Special notes

When selecting the *Tyrosine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tyrosine	3	2	3

Second-stage model

For differentiation of the substance/substance group *Tyrosine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tyrosine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Tyrosine	13G24-N22	21574	60	1411030
Fagron	Tyrosine	16B26-B01-322911	23533	40	20160324
Fagron	Tyrosine	18E15-B02-359934	24692	40	20181001

Validation samples

A total of 341078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 140 spectra of 3 reference samples from the substance/substance group *Tyrosine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110549 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 100 spectra of 2 reference samples from the substance/substance group *Tyrosine*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Tyrosine	L1401037-01	21586	60
Fagron	Tyrosine	17B06-B03-338139	24008	40

- 119042 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 3 spectra from 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Tyrosine*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Tyrosine	L1506022-02	1
Euro OTC	Tyrosine	L1401037	1
Euro OTC	Tyrosine	L1210050-01	1

- 111244 spectra from 742 *Apo-Ident* customers from a total of 31888 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tyrosine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tyrosine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	140	0	110549
Type B	0	100	0	119042
Type C	0	2	1	111244

The substance/substance group *Tyrosine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 99.8903 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Tyrosine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Glycine	44.03	—
Theophylline-ethylenediamine hydrate	45.13	—
Levocarnitine	45.78	—
Miconazole nitrate	53.59	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tyrosine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24692	21574	7.98	73.31
21574	21574	0.00	72.71
23533	21574	5.89	72.84

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Tyrothricin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20732-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Tyrothricin; Tyrothricinum

Special notes

When selecting the *Tyrothricin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tyrothricin	2	1	12

Second-stage model

For differentiation of the substance/substance group *Tyrothricin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Tyrothricin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Fagron	Tyrothricin	12K14-N01	20732	40	1509178
Fagron	Tyrothricin	12K14-N01	21683	60	AR-15-FG-001172-01
Fagron	Tyrothricin	14A23-B05-294146	21876	60	AR-15-FG-015005-01

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Tyrothricin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 110 529 spectra from a total of 1964 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 146 spectra of 3 reference samples from the substance/substance group *Tyrothricin*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Fagron	Tyrothricin	17E09-B03-341231	23742	40
Fagron	Tyrothricin	12K14-N01	21683SI [†]	60
Fagron	Tyrothricin	14A23-B05-294146	21876SI [†]	46

- 118 996 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 19 spectra from 11 *Apo-Ident* customers from 12 batches from the substance/substance group *Tyrothricin*.
- Among them are spectra of independent samples from 12 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Fagron	Tyrothricin	13A14-N04	1
Fagron	Tyrothricin	17E09-B03	1
Fagron	Tyrothricin	17E09-B03-352743	4
Fagron	Tyrothricin	17E09-B03-341231	1
Fagron	Tyrothricin	17E09-B03-351982	1
Fagron	Tyrothricin	15A06-B02-303893	1
Fagron	Tyrothricin	15A06-B02-3005	1
Fagron	Tyrothricin	17E09B03352743	1
Fagron	Tyrothricin	17E09-B03-350209	1
Fagron	Tyrothricin	15a06-B02-323005	1
Fagron	Tyrothricin	15A06-B02-323005	5
Fagron	Tyrothricin	B2500226	1

- 111 228 spectra from 742 *Apo-Ident* customers from a total of 31 879 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Tyrothricin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tyrothricin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	141	5	118 996
Type C	0	19	0	111 228

The substance/substance group *Tyrothricin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	96.5753 % (> 94.5205 %)
Type C	100.0000 % (> 99.8899 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ty-rothricin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Morphine sulfate	29.34	—
Gramicidin	34.67	—
Polymyxin B sulfate	35.11	—
Prednisone	35.84	—
Prednisolone acetate	36.81	—
Riboflavin	39.15	—
Triamcinolone, micronized	48.16	—
Magnesium citrate	48.47	—
Ambroxol hydrochloride	50.19	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ty-rothricin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20732	20732	0.00	37.54
21683	21683	0.00	36.12
21876	21876	0.00	36.00

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances,

thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Ubidecarenone**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20392-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Ubidecarenone; Ubidecarenonum

Special notes

When selecting the *Ubidecarenone* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ubidecarenone	9	5	21

Second-stage model

For differentiation of the substance/substance group *Ubidecarenone* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Ubidecarenone*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Ubidecarenone	14004504	21388	60	AR-15-FG-009220-01
Caelo	Ubidecarenone	17209402	23580	40	20170823
Caelo	Ubidecarenone	17209402	23581	40	20170823
Caelo	Ubidecarenone	172094	23647	35	20170823*
Euro OTC	Ubidecarenone	1205029-01	21247	40	20121009
Euro OTC	Ubidecarenone	1605030	22696	40	20160623*
Euro OTC	Ubidecarenone	1703026	23127	40	20170406*
Euro OTC	Ubidecarenone	1801019	23881	40	20180126*
Fagron	Ubidecarenone	16G26-B01-331742	23161	40	20170110
Fagron	Ubidecarenone	18J24-B01-357225	24688	40	20181121

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 415 spectra of 10 reference samples from the substance/substance group *Ubidecarenone*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 274 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- 200 spectra of 5 reference samples from the substance/substance group *Ubidecarenone*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Ubidecarenone	182298	24281	40
Euro OTC	Ubidecarenone	1802025	24074	40
Euro OTC	Ubidecarenone	1804020	24116	40
Euro OTC	Ubidecarenone	1810012	24305	40
Euro OTC	Ubidecarenone	1902030	24630	40

- 118 942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 30 spectra from 14 *Apo-Ident* customers from 22 batches from the substance/substance group *Ubidecarenone*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Ubidecarenone	APSZFQ150614C	1
Audor Pharma	Ubidecarenone	APSCFQ150614C	1
Audor Pharma	Ubidecarenone	APSZFQ170617C	1
Caelo	Ubidecarenone	18048401	1
Dr. Behr	Ubidecarenone	WE18020018	1
Euro OTC	Ubidecarenone	1801019-01	1
Euro OTC	Ubidecarenone	1902030-01	2
Euro OTC	Ubidecarenone	1605030-01	3
Euro OTC	Ubidecarenone	1802025-01	2
Euro OTC	Ubidecarenone	1403020-02	1
Euro OTC	Ubidecarenone	1014E-07029	1
Euro OTC	Ubidecarenone	1515M-07029	1
Euro OTC	Ubidecarenone	L1403020-01	1
Fagron	Ubidecarenone	14H26-B04-298244	1
Fagron	Ubidecarenone	14E12-B06-293861	1
Fagron	Ubidecarenone	16G26-B01-344334	2
Fagron	Ubidecarenone	18a16-b03-351350	1
Fagron	Ubidecarenone	18A16-B03-351350	1
Fagron	Ubidecarenone	18A16-B03	2
Fagron	Ubidecarenone	18J24-B01	1
Fagron	Ubidecarenone	16G26-B01	3
Fagron	Ubidecarenone	16B10-B05-327606	1

- 111 217 spectra from 742 *Apo-Ident* customers from a total of 31 869 batches from a further 706

substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Ubidecarenone* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ubidecarenone* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	415	0	110 274
Type B	0	200	0	118 942
Type C	0	30	0	111 217

The substance/substance group *Ubidecarenone* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.5542 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 80.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ubidecarenone* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Finasteride (form III)	55.51	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ubidecarenone* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24688	23127	2.35	62.66
21247	23881	2.45	62.74
21388	21388	0.00	61.02
22696	22696	0.00	62.50
23127	23127	0.00	62.43
23161	23127	1.73	62.34
23580	21388	2.84	60.94
23581	21388	1.94	61.61
23647	23647	0.00	59.83
23881	23881	0.00	63.31

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Urea**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20017-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Urea; Carbamidum

Special notes

When selecting the *Urea* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Urea	9	8	354

Second-stage model

For differentiation of the substance/substance group *Urea* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Urea*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Urea	15154103	22315	60	20150722
Caelo	Urea	15154103	22315SI	60	20150722
Caelo	Urea	161074	22466	60	20160509*
Caelo	Urea	170216	23033	40	20170202*
Caelo	Urea	18023003	24294	40	20180216
Euro OTC	Urea	1404024-01	21537	60	20140519
Euro OTC	Urea	1601044	22376	40	20160208*
Euro OTC	Urea	1604044	22552	40	20160512*
Fagron	Urea	12F25-N05	20712	40	20120724
Fagron	Urea	14I18-B03-303581	22317	60	20141003
Fagron	Urea	14I18-B03-303581	22317SI	60	20141003

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 560 spectra of 11 reference samples from the substance/substance group *Urea*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 9 different batches.
- 110 129 spectra from a total of 1957 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 560 spectra of 14 reference samples from the substance/substance group *Urea*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Urea	180242	24042	40
Caelo	Urea	180230	24043	40
Caelo	Urea	190316	24550	40
Euro OTC	Urea	1702023	23156	40
Euro OTC	Urea	1707015	23535	40
Euro OTC	Urea	1804007	24078	40
Euro OTC	Urea	1811012	24340	40
Euro OTC	Urea	1908016	24865	40
Caelo	Urea	170216	23033SI [†]	40
Caelo	Urea	18023003	24294SI [†]	40
Euro OTC	Urea	1604044	22552SI [†]	40
Euro OTC	Urea	1702023	23156SI	40
Euro OTC	Urea	1804007	24078SI	40
Euro OTC	Urea	1811012	24340SI	40

- 118 582 spectra from a total of 2409 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2832 spectra from 643 *Apo-Ident* customers from 368 batches from the substance/substance group *Urea*.
- Among them are spectra of independent samples from 352 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
ACM	Urea	KNC1795J14	1
ACM	Urea	KNC0557J15	3
ACM	Urea	KNC0236J16	2
AHC	Urea	15154110	1
Caelo	Urea	18023019	2
AHD	Urea	14E07-B05-293469	1
AHD	Urea	3514E-02544	1
Alliance health	Urea	14E07-B05-297167	1
Alliance Healthcare	Urea	12111823	1
anzag	Urea	14E07-B05-293469	1
Anzag	Urea	12111801	1
Anzag	Urea	16107411	1
Anzag / Noweda	Urea	13064206	1
Anzag 17.04.13 ek:6,84EUR	Urea	12111823	1
Fagron	Urea	14E8900-0001	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Urea	18109801	1
Anzag/Henry Lamotte	Urea	13-18-B03-303581	1
Audor Pharma	Urea	PU145	1
Beiersdorf	Urea	15154112	1
Beiersdorf AG	Urea	14/18-B03-303576	1
Beyvers/AHD	Urea	15087104	1
Bombastus	Urea	1601044-01	1
Bombastus	Urea	16107424	2
Bombastus	Urea	1707015-01	1
Bombastus	Urea	14107108	1
Bombastus	Urea	15087107	1
Bombastus	Urea	18023012	1
Bombastus	Urea	11150721	1
Bombastus	Urea	1804007-01	1
Bombastus	Urea	18023004	1
Caelo	Urea	1211806	1
Caelo	Urea	13064223	33
Caelo	Urea	4116M-02544	1
Caelo	Urea	1234	1
Caelo	Urea	123566	1
Caelo	Urea	13064226	13
Caelo	Urea	11150722	3
Caelo	Urea	11150736	4
Caelo	Urea	12111802	8
Caelo	Urea	10081208	1
Caelo	Urea	11150721	1
Caelo	Urea	2109212544	1
Caelo	Urea	12111808	9
Caelo	Urea	11150702	2
Caelo	Urea	10116	1
Caelo	Urea	21111806	1
Caelo	Urea	12111810	13
Caelo	Urea	4111M-02544	1
Caelo	Urea	10169726	2
Caelo	Urea	12111807	5
Caelo	Urea	12111809	12
Caelo	Urea	20130912-4	1
Caelo	Urea	12111822	15
Caelo	Urea	10169722	1
Caelo	Urea	30031304	1
Caelo	Urea	3012A-02544	1
Caelo	Urea	12L10-N08	1
Caelo	Urea	12111826	6
Caelo	Urea	21051304	1
Caelo	Urea	1211820	1
Caelo	Urea	123456	4
Caelo	Urea	13064203	11
Caelo	Urea	13064206	18
Caelo	Urea	1211809	1
Caelo	Urea	26071304	1
Caelo	Urea	13064212	23
Caelo	Urea	1364212	1
Caelo	Urea	17101310	1
Caelo	Urea	1306412	1
Caelo	Urea	9240908	1
Caelo	Urea	22111305	1
Caelo	Urea	13064224	2
Caelo	Urea	17011405	1
Caelo	Urea	13064221	6
Caelo	Urea	13064227	5

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Supplier	Substance	Batch	Spectra
Caelo	Urea	5061410	1
Caelo	Urea	13064231	9
Caelo	Urea	14E07-B05-293469	1
Caelo	Urea	14107101	9
Caelo	Urea	14107109	20
Caelo	Urea	14011513	1
Caelo	Urea	14107112	16
Caelo	Urea	14107117	10
Caelo	Urea	20031514	1
Caelo	Urea	13042015B	1
Caelo	Urea	14107119	21
Caelo	Urea	14107120	9
Caelo	Urea	14107122	16
Caelo	Urea	15087102	7
Caelo	Urea	15087103	20
Caelo	Urea	13072015B	1
Caelo	Urea	25082015A	1
Caelo	Urea	14/18-B03-303581	2
Caelo	Urea	15087110	23
Caelo	Urea	Validierungsmessung	1
Caelo	Urea	15154104	80
Caelo	Urea	2738	1
Caelo	Urea	15154107	22
Caelo	Urea	15154110	36
Caelo	Urea	160125/2	1
Caelo	Urea	15154101	1
Caelo	Urea	151541	2
Caelo	Urea	2/20141507	1
Caelo	Urea	2416I-02544	1
Caelo	Urea	14I18-B03-303581	1
Caelo	Urea	15154112	39
Caelo	Urea	1514110	2
Caelo	Urea	151154112	1
Caelo	Urea	160620UP	1
Caelo	Urea	1236	1
Caelo	Urea	16107407	31
Caelo	Urea	151541111	1
Caelo	Urea	16107405	9
Caelo	Urea	16107411	30
Caelo	Urea	16107413	9
Caelo	Urea	15145112	1
Caelo	Urea	1517E-02544	1
Caelo	Urea	19041703	1
Caelo	Urea	17021601	4
Caelo	Urea	1222	1
Caelo	Urea	16107417	26
Caelo	Urea	161074165325	1
Caelo	Urea	1604044-01	1
Caelo	Urea	16107419	18
Caelo	Urea	6101703	1
Caelo	Urea	16107428	25
Caelo	Urea	1707015-01	2
Caelo	Urea	1802402	1
Caelo	Urea	21041802	1
Caelo	Urea	1061801	1
Caelo	Urea	1803003	1
Caelo	Urea	180223003	1
Caelo	Urea	18023012	48
Caelo	Urea	19031605	12
Caelo	Urea	18023022	1

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Supplier	Substance	Batch	Spectra
Caelo	Urea	1211808	1
Caelo	Urea	1610743	1
Caelo	Urea	11150725	3
Caelo	Urea	18023004	86
Caelo	Urea	13064215	22
Caelo	Urea	19031610	4
Caelo	Urea	15087105	11
Caelo	Urea	1610407	1
Caelo	Urea	170509UP/16107407	1
Caelo	Urea	118023004	1
Caelo	Urea	14197118	1
Caelo	Urea	10038587	2
Caelo	Urea	10038593	1
Caelo	Urea	15087107	17
Caelo	Urea	14107424	1
Caelo	Urea	16107420	42
Caelo	Urea	18023010	35
Caelo	Urea	16107408	1
Caelo	Urea	13064213	5
Caelo	Urea	2324534	1
Caelo	Urea	180322H/18024202	1
Caelo	Urea	16107422	31
Caelo	Urea	18023003-20180830Ma2	1
Caelo	Urea	1514112	1
Caelo	Urea	16107418	24
Caelo	Urea	16107427	1
Caelo	Urea	15154113	24
Caelo	Urea	84 (18023010)	1
Caelo	Urea	85 (18023012)	2
Caelo	Urea	14107103	8
Caelo	Urea	1508/104	1
Caelo	Urea	16I13-B02-332953	1
Caelo	Urea	16/13-B02-332593	1
Caelo	Urea	18G04-B03-353339	1
Caelo	Urea	2016142709	1
Caelo	Urea	16107406	21
Caelo	Urea	13064202	12
Caelo	Urea	13E21-N05	1
Caelo	Urea	13064228	22
Caelo	Urea	5100	1
Caelo	Urea	1823004	1
Caelo	Urea	3270	1
Caelo	Urea	3357	1
Caelo	Urea	11150738	1
Caelo	Urea	13064233	15
Caelo	Urea	12111804	4
Caelo	Urea	1407109	1
Caelo	Urea	13064201	6
Caelo	Urea	11150703	1
Caelo	Urea	10823004	1
Caelo	Urea	19031609	3
Caelo	Urea	19031615	1
Caelo	Urea	16107248	1
Caelo	Urea	17321206	1
Caelo	Urea	12111823	9
Caelo	Urea	13064207	18
Caelo	Urea	13064217	1
Caelo	Urea	13064236	8
Caelo	Urea	1317B02-287602	1
Caelo	Urea	4914I-02544	1

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Supplier	Substance	Batch	Spectra
Caelo	Urea	16107424	54
Caelo	Urea	14107102	27
Caelo	Urea	18023006	41
Caelo	Urea	18023018	11
Caelo	Urea	19031604	16
Caelo	Urea	1113A-025	1
Caelo	Urea	12111820	12
Caelo	Urea	11150714	1
Caelo	Urea	14107113	17
Caelo	Urea	568900	1
Caelo	Urea	1514107	1
Caelo	Urea	16107423	11
Caelo	Urea	18023001	12
Caelo	Urea	18203012	1
Caelo	Urea	19031606	7
Caelo	Urea	1824202	1
Caelo	Urea	107063	1
Caelo	Urea	14I18-B03	1
Caelo	Urea	18024202	36
Caelo	Urea	12111834	3
Caelo	Urea	13064214	13
Caelo	Urea	15087104	16
Caelo	Urea	15154116	13
Caelo	Urea	16107412	75
Caelo	Urea	1802003	1
Caelo	Urea	1702023-01	2
Caelo	Urea	14107428	1
Caelo	Urea	18024201	36
Caelo	Urea	18023007	25
Caelo	Urea	1804007-01	1
Caelo	Urea	18023016	5
Caelo	Urea	12111828	19
Caelo	Urea	4013Q2544	1
Caelo	Urea	14E07-B05-289706	1
Caelo	Urea	15154109	8
Caelo	Urea	161072422	1
Caelo	Urea	1607422	1
Caelo	Urea	12111801	4
Caelo	Urea	314Q2544	1
Caelo	Urea	14107108	10
Caelo	Urea	1515404	1
Caelo	Urea	2116A-02544	1
Caelo	Urea	16D22-B02-322526	1
Caelo	Urea	16107416	15
Caelo	Urea	16107426	18
Caelo	Urea	16107429	8
Caelo	Urea	1802401	1
Caelo	Urea	19031611	2
Caelo	Urea	1211804	1
Caelo	Urea	13064230	15
Caelo	Urea	14107118	7
Caelo	Urea	16107425	6
Caelo	Urea	18023011	47
Caelo	Urea	18023015	39
Caelo	Urea	AKD6	1
Caelo	Urea	17107429	1
Caeolo/Gehe	Urea	16107424	1
Caeolo/Noweda	Urea	14107112	1
Caesar & Loretz	Urea	18024201	1
Caesar & Loretz	Urea	18023004	1

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Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Urea	12111822	1
Caesar & Loretz GmbH	Urea	13064206	1
Caesar & Loretz GmbH	Urea	1306421	1
Caesar & Loretz GmbH	Urea	13064223	1
Caesar & Loretz GmbH	Urea	15087105	1
Caesar & Loretz GmbH	Urea	15087103	1
Caesar & Loretz GmbH	Urea	15154104	1
Caesar & Loretz GmbH	Urea	16107411	1
Caesar & Loretz GmbH	Urea	18023004	1
Caesar & Loretz GmbH	Urea	18023011	1
Caesar & Loretz GmbH	Urea	18023012	1
Caesar & Loretz GmbH	Urea	18023015	5
Caesar & Loretz GmbH	Urea	18023019	1
Caesar & Loretz GmbH	Urea	18023018	1
Caesar & Loretz GmbH	Urea	19031604	2
Caesar & Loretz GmbH	Urea	19031603	2
Caesar & Loretz GmbH	Urea	19031606	2
Caesar & Loretz GmbH	Urea	19031616	1
Caesar & Loretz GmbH	Urea	19031615	1
Caesar & Loretz GmbH / ...	Urea	15154111	1
Caesar & Loretz GmbH / ...	Urea	16107417	1
Caesar & Loretz GmbH / ...	Urea	17347901	1
Caesar & Loretz GmbH / ...	Urea	18023003	1
Caesar & Loretz GmbH, 4...	Urea	11150736	1
Caesar & Loretz GmbH, 4...	Urea	12111804	1
Caesar & Loretz GmbH, 4...	Urea	12111810	2
Caesar & Loretz GmbH, 4...	Urea	12111828	2
Caesar & Loretz GmbH, 4...	Urea	12111822	1
Caesar & Loretz GmbH, 4...	Urea	13064206	2
Caesar & Loretz GmbH, 4...	Urea	13064212	3
Caesar & Loretz GmbH/ F...	Urea	19031604	1
Caesar & Loretz GmbH/An...	Urea	18023018	1
Caesar & Loretz GmbH/Fi...	Urea	18023015	1
Caesar & Loretz GmbH/Ge...	Urea	18023019	1
Caesar & Loretz/AHD	Urea	18023007	2
Caesar & Loretz/Gehe	Urea	19031606	1
Caesar & Loretz GmbH	Urea	13064203	1
Caesar u Loretz	Urea	12111828	1
Caesar&Loretz	Urea	16107428	1
Caesar&Loretz GmbH	Urea	14107101	1
Caesar&Loretz GmbH	Urea	15154111	1
Caesar&Loretz GmbH	Urea	16107417	1
Caesar&Loretz GmbH /Anzag	Urea	14107113	1
Caesar&Loretz GmbH /Anzag	Urea	15087110	1
Caesar&Loretz GmbH D-40...	Urea	12111808	2
Caesar&Loretz GmbH,Phön...	Urea	16107411	1
Caesar&Loretz GmbH/ San...	Urea	18023001	2
Caesar&Loretz GmbH/Anzag	Urea	13064217	1
Caesar&Loretz GmbH/Anzag	Urea	13064231	1
Caesar&lorenz,Anzag	Urea	11150738	1
Caesar&lorenz,Phoenix	Urea	11150713	1
Caesar&lorenz,Phoenix	Urea	12111806	3
Caesar&Loretz/Caesar&Lo...	Urea	15154104	1
Caesar/Lorenz	Urea	12111822	1
Caesar/Noweda	Urea	12111823	1
Caesar/Noweda	Urea	13064208	1
Caesar und Loretz GmbH	Urea	18023018	1
Calo/AHD	Urea	15154104	1
Castor/Phönix	Urea	15154104	1
Cealo	Urea	16107416	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Cealo/Phönix	Urea	13064231	1
Ceasar & Loretz GmbH / ...	Urea	16107422	2
Cordes/Noweda	Urea	17021601	1
Dan Pharma	Urea	D08118	1
Delta	Urea	18023004	1
Dr. August Wolff	Urea	13E17N02	1
Dr.Wolff	Urea	1234567	1
Eur	Urea	1707015-01	1
Eurho	Urea	1404024-01	1
EuRho	Urea	1212007-01	1
EuRho	Urea	150304201	1
EuRho	Urea	1702023-01	1
EuRho	Urea	1707015-01	1
EuRho/Noweda	Urea	1707015-01	1
Euro OTC	Urea	1601044-01	26
Euro OTC	Urea	V076-2016	1
Euro OTC	Urea	1110023-01	1
Euro OTC	Urea	13064239	1
Euro OTC	Urea	14107101	2
Euro OTC	Urea	15154103	2
Euro OTC	Urea	15154104	3
Euro OTC	Urea	160404401	2
Euro OTC	Urea	1707015-01	28
Euro OTC	Urea	18040701	1
Euro OTC	Urea	72/14	1
Euro OTC	Urea	150304201	1
Euro OTC	Urea	1604044-01	26
Euro OTC	Urea	160104401	1
Euro OTC	Urea	1804007-01	29
Euro OTC	Urea	1503042-01	25
Euro OTC	Urea	1515404	1
Euro OTC	Urea	16107412	3
Euro OTC	Urea	170202301	3
Euro OTC	Urea	180400701	1
Euro OTC	Urea	1811012-01	20
Euro OTC	Urea	1908016-01	3
Euro OTC	Urea	14107108	1
Euro OTC	Urea	18023015	1
Euro OTC	Urea	1804007-1	1
Euro OTC	Urea	1212007-01	6
Euro OTC	Urea	15154107	2
Euro OTC	Urea	UP250171017	1
Euro OTC	Urea	1804007-02	3
Euro OTC	Urea	170701501	2
Euro OTC	Urea	1212007-02	3
Euro OTC	Urea	16I13-B02-332953	1
Euro OTC	Urea	1702023-01	25
Euro OTC	Urea	V038-2017	1
Fagron	Urea	11H01-N08	2
Fagron	Urea	11F24-N16	1
Fagron	Urea	12I04-N06	1
Fagron	Urea	12110-n08	1
Fagron	Urea	12104-N06	1
Fagron	Urea	3613M-02544	1
Fagron	Urea	13E17-N02	1
Fagron	Urea	13J17-B02-287604	5
Fagron	Urea	13J17-B02-287602	2
Fagron	Urea	13J17-B02	2
Fagron	Urea	13L20B03	1
Fagron	Urea	14E07B05	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Urea	14E07-B07-293469	1
Fagron	Urea	14E07-B05-297165	3
Fagron	Urea	2014162937	3
Fagron	Urea	14I18-B03	4
Fagron	Urea	14I18-B03-303581	1
Fagron	Urea	14I18-B03-0303581	1
Fagron	Urea	14/18-B03-303581	7
Fagron	Urea	14/18-B03-303576	1
Fagron	Urea	13/17-1302-287602	1
Fagron	Urea	1418b03303581	1
Fagron	Urea	1418B03303581	1
Fagron	Urea	14I18-B03	1
Fagron	Urea	18-B03-303581	1
Fagron	Urea	B03-303581	1
Fagron	Urea	13064233	1
Fagron	Urea	9K27-M01	1
Fagron	Urea	16D22-B02	3
Fagron	Urea	16D22-B02-322532	4
Fagron	Urea	16D22-B02-3221532	1
Fagron	Urea	16D22-B02-322426	1
Fagron	Urea	16D22-B02-326481	7
Fagron	Urea	7L17-N01	1
Fagron	Urea	16/13-B02-330166	1
Fagron	Urea	16107422	1
Fagron	Urea	16/13-B02	1
Fagron	Urea	1707015-01	1
Fagron	Urea	16/13-B02-332953	1
Fagron	Urea	1613b02332953	1
Fagron	Urea	17H16-B01	3
Fagron	Urea	18A24-B07-352707	2
Fagron	Urea	18G04-B03-353339	3
Fagron	Urea	18023012	1
Fagron	Urea	12L10-N08	5
Fagron	Urea	14E07-B05-293469	9
Fagron	Urea	17H16-B01-340516	1
Fagron	Urea	1211822	1
Fagron	Urea	18G04-B03-355378	1
Fagron	Urea	15154104	2
Fagron	Urea	18G04-B03-35339	1
Fagron	Urea	16I13-B02-330166	2
Fagron	Urea	18A24-B07-346692	1
Fagron	Urea	16I13-B02-328152	2
Fagron	Urea	18A24-B07-347410	1
Fagron	Urea	18G04-B03	1
Fagron	Urea	2016142709	3
Fagron	Urea	16D22-B02-322526	3
Fagron	Urea	16I13-B02	1
Fagron	Urea	17H16-B01-342080	2
Fagron	Urea	18A24-B07-349015	2
Fagron	Urea	18A24-B07-351975	3
Fagron	Urea	13D03-N001	1
Fagron	Urea	13D03-N01	9
Fagron	Urea	13E21-N05	2
Fagron	Urea	14/18B03303581	1
Fagron	Urea	16D22-802-326481	1
Fagron	Urea	2018163455	1
Fagron	Urea	16I13-B02-332953	1
Fagron	Urea	13L20-B03_289708	1
Fagron	Urea	14I18-B03-303576	5
Fagron	Urea	14E07-B05	8

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Urea	14E-07-B05-293469	1
Fagron	Urea	16107418	1
Fagron	Urea	18023015	2
Fagron	Urea	14107117	1
Fagron	Urea	14E07B05293469	1
Fagron	Urea	13L20-B03-289708	6
Fagron	Urea	14E07-B05-289706	1
Fagron	Urea	13J17B02-287604	1
Fagron	Urea	15154112	1
Fagron	Urea	1613-B02-328152	2
Fagron	Urea	18023006	1
Fagron	Urea	18A24-B07	1
Fagron	Urea	12C20-N05	1
Fagron	Urea	235/12I04-N06	1
Fagron	Urea	11C25-N01	1
Fargon	Urea	14e07-b05-297165	1
Fargon/Alliance HC	Urea	14E07-B05-293469	1
Fiebig	Urea	15087103	1
Fiebig	Urea	15154112	1
Fiebig	Urea	16107411	1
Fiebig	Urea	16107417	1
Fiebig	Urea	16107425	1
Fiebig	Urea	16107428	1
Fiebig	Urea	18024201	1
Fiebig	Urea	18023010	1
Fiebig	Urea	18023018	2
Finteler Apotheke	Urea	16107417	1
Finze	Urea	1264	1
Gatt-Koller	Urea	1800697	1
Gatt-Koller	Urea	1803268	3
gehe	Urea	16107425	1
Gehe	Urea	12111810	1
Gehe	Urea	12111808	1
Gehe	Urea	12111822	1
Gehe	Urea	12111826	1
Gehe	Urea	13064232	1
Gehe	Urea	14107112	1
Gehe	Urea	15087103	1
Gehe	Urea	15087107	2
Gehe	Urea	15154112	1
Gehe	Urea	16107412	2
Gehe	Urea	16107422	2
Gehe	Urea	16107428	1
Gehe	Urea	10038593	1
Gehe	Urea	18023004	2
Gehe	Urea	18023011	1
Gehe	Urea	1804007-01	1
Gehe	Urea	18023015	2
Gehe	Urea	19031604	1
Gehe	Urea	18023018	1
Gehe	Urea	19031606	1
GEHE	Urea	16107412	1
GEHE	Urea	16107416	1
GEHE	Urea	16107422	1
GEHE	Urea	18023007	1
Gehe am 11.10.2017	Urea	16107419	1
Gehe,05.04.17, 5,30EUR	Urea	16107412	1
Caelo	Urea	1241017	1
Gehe/Fragon	Urea	16D22-B02-326481	1
Gutenberg-Apotheke	Urea	13064227	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Hirsch	Urea	810811	1
Caelo	Urea	1306422	1
Ichthyol/Phoenix	Urea	15154104	1
Infectopharm/Phönix	Urea	18023011	1
Jenne	Urea	18023018	1
Kehr	Urea	16107418	1
Kehr	Urea	18023004	1
Kehr	Urea	1802007	1
Euro OTC	Urea	16107428	1
Kirsch Pharma GmbH/Noweda	Urea	14E07-B05-293469	1
Fagron	Urea	14E07-B05-297167	5
krieger	Urea	19031604	1
Krieger	Urea	15154110	1
L12	Urea	16107418	1
L30	Urea	16107407	1
L30	Urea	16107424	1
L30	Urea	18023011	1
Laborchemie Apolda/Jenn...	Urea	12345	1
Löns Apotheke	Urea	20349	1
Löns Apotheke	Urea	40003	1
Noveda	Urea	19031610	1
Noweda	Urea	11150714	1
Noweda	Urea	4109M-02544	1
Noweda	Urea	13064223	1
Noweda	Urea	14107101	1
Noweda	Urea	15154110	1
Noweda	Urea	15154112	1
Noweda	Urea	16107419	3
Noweda	Urea	16107422	1
Noweda	Urea	16107416	1
Noweda	Urea	18024201	1
Noweda	Urea	18023004	1
Noweda	Urea	18023015	1
Noweda	Urea	19031611	1
Noweda 02.08.2019	Urea	18023018	1
Noweda 02.09.2019	Urea	18023019	1
Caelo	Urea	5208	1
Caelo	Urea	15154111	41
Caelo	Urea	19031603	1
Noweda/KremerGmbH	Urea	13064201	1
Euro OTC	Urea	18024201	1
Ph.Eur.7.0	Urea	14107109	1
Phoenix	Urea	13064231	1
Phoenix	Urea	15154113	1
Phoenix	Urea	16107411	1
Phoenix	Urea	16107420	1
Phoenix	Urea	16107428	1
Phoenix	Urea	18024201	2
Phoenix	Urea	18023004	2
Phoenix	Urea	3201	1
Phoenix	Urea	18023006	2
Phoenix	Urea	18023012	1
Phoenix	Urea	19031605	1
PHOENIX 02.05.2014	Urea	13J17-B02-287602	2
Phoenix 17.2.2014	Urea	13064227	1
Phoenix 31.07.19	Urea	18023001	1
Caelo	Urea	12111803	1
Caelo	Urea	13064239	2
phönix	Urea	15154111	1
phönix	Urea	15154103	2

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continued from previous page

Supplier	Substance	Batch	Spectra
phönix	Urea	15154112	2
phönix	Urea	16107412	2
phönix	Urea	16107420	1
Phönix	Urea	12111822	1
Phönix	Urea	13064207	1
Phönix	Urea	13064215	1
Phönix	Urea	13064223	1
Phönix	Urea	13064236	1
Phönix	Urea	14107109	1
Phönix	Urea	15087110	1
Phönix	Urea	15154113	1
Phönix	Urea	123456	1
Phönix	Urea	16107412	2
Phönix	Urea	16107419	1
Phönix	Urea	16107424	1
Phönix	Urea	18023003	1
Phönix	Urea	18023006	1
Phönix	Urea	18023004	1
Phönix	Urea	18023010	1
PHÖNIX	Urea	18023001	1
Phönix Gotha	Urea	13064202	1
Phönix Gotha	Urea	1212007-01	1
Phönix Gotha	Urea	V096/2012	1
Phönix Gotha	Urea	1404024-01	1
Euro OTC	Urea	16107411	1
Phönix/Gehe	Urea	18024201	2
Raben-Apotheke Mildenau	Urea	13J17-B02-287604	2
Raben-Apotheke Mildenau	Urea	13J17-Bo2-287604	1
Sanacorp	Urea	12111808	2
Sanacorp	Urea	12111810	1
Sanacorp	Urea	12111820	1
Sanacorp	Urea	1110023-01	1
Sanacorp	Urea	13064203	1
Sanacorp	Urea	13064212	1
Sanacorp	Urea	13064223	1
Sanacorp	Urea	1212007	1
Sanacorp	Urea	62/AKD50s	1
Sanacorp	Urea	63/AKD1	1
Sanacorp	Urea	14107102	1
Sanacorp	Urea	1405028-01	1
Sanacorp	Urea	14107112	1
Sanacorp	Urea	16107418	2
Sanacorp	Urea	16107423	1
Sanacorp	Urea	18024202	1
Sanacorp	Urea	18023004	1
Sanacorp	Urea	18023007	1
Caelo	Urea	11150713	1
Caelo	Urea	12111806	5
Caelo	Urea	62/AKD49	1
Caelo	Urea	63/AKD4	1
Spangro 07.02.2014	Urea	13064226	1
Spangro 17.01.2019	Urea	18023007	1
Spangro 22.05.2014	Urea	13064230	1
Spangro_07.11.2018	Urea	18023010	1
Caelo	Urea	13064232	14
test	Urea	test	1
THC/Phönix	Urea	18023006	1
Träger	Urea	14107112	1
VDL;05.02.15;10.15EUR	Urea	14107113	1
WE:Phoenix 11.08.16 E...	Urea	15154111	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Urea	15154103	47
	Urea	12111808	1
Caelo	Urea		7
Caelo	Urea	161074	2
Caelo	Urea	18023003	39
Euro OTC	Urea	1404024-01	12
Euro OTC	Urea		2
Fagron	Urea	12F25-N05	5
Fagron	Urea	14I18-B03-303581	3
Gutenberg-Apotheke	Urea		1
PHOENIX 29.08.2014	Urea		1

- 108 415 spectra from 741 *Apo-Ident* customers from a total of 31 535 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Urea* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Urea* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	560	0	110 129
Type B	0	552	8	118 582
Type C	0	2766	66	108 415

The substance/substance group *Urea* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.9286 %)
Type B	100.0000 % (> 99.9893 %)	98.5714 % (> 98.0357 %)
Type C	100.0000 % (> 99.8899 %)	97.6695 % (> 97.5636 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Urea* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oxalic acid	42.26	—
Bismuth gallath, basic	46.32	—
Levothyroxin sodium	58.87	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Urea* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22552	22552	0.00	43.20
20712	22552	1.82	43.01
21537	22466	2.30	44.80
22315	22552	3.86	42.11
22317	22376	3.65	42.28
22376	22376	0.00	43.33
22466	22466	0.00	43.81
23033	23033	0.00	43.18
24294	22552	6.02	41.50

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Uridine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20744-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Uridine; Uridinum

Special notes

When selecting the *Uridine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Uridine	3	1	22

Second-stage model

For differentiation of the substance/substance group *Uridine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Uridine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Uridine	APIB160018211AU	23529	40	20161118
Fagron	Uridine	11G07-N04	20744	60	1402481
Fagron	Uridine	13K18-B31-288497	21895	60	20131129

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 160 spectra of 3 reference samples from the substance/substance group *Uridine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 529 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Uridine*.
- Among them are spectra of independent samples from 1 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Audor Pharma	Uridine	APIB1600169AU	23507	40
Audor Pharma	Uridine	APIB1600169AU	23507SI	40
Audor Pharma	Uridine	APIB160018211AU	23529SI [†]	40

- 119 022 spectra from a total of 2418 batches from further 799 substances. These spectra were

recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 79 spectra from 32 *Apo-Ident* customers from 23 batches from the substance/substance group *Uridine*.
- Among them are spectra of independent samples from 21 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Audor Pharma	Uridine	AP721060040/5U	2
Audor Pharma	Uridine	APIB1600182AU	7
Audor Pharma	Uridine	APIB1600169AU	26
Audor Pharma	Uridine	APIB1600169AU/Re	1
Audor Pharma	Uridine	AP30514U	4
Audor Pharma	Uridine	APIB1400280AU	1
Audor Pharma	Uridine	APIB16001169	1
Audor Pharma	Uridine	AP30514IB1500001AXU	4
Audor Pharma	Uridine	APIB1600169	1
Aufor/AHD	Uridine	AP30514IB1500001AXU	1
Euro OTC	Uridine	APIB1600169AU	2
Fagron	Uridine	22041301	1
Fagron	Uridine	16101301	1
Fagron	Uridine	13D08-N26	1
Fagron	Uridine	14051405	1
Fagron	Uridine	721110090	4
Fagron	Uridine	12091402	1
Fagron	Uridine	13K18-B31	4
Fagron	Uridine	14F02-B09	1
Fagron	Uridine	13D29-N06	3
Fagron	Uridine	14F02-B09-305467	7
Phönix	Uridine	721010040	1
Sanacorp	Uridine	AP721060040/5U	1
siehe WE-Prüfprotokoll	Uridine	54/11	1
Audor Pharma	Uridine		1
Fagron	Uridine	11G07-N04	1

- 111 168 spectra from 742 *Apo-Ident* customers from a total of 31 868 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Uridine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Uridine* and it was evaluated how

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	160	0	110 529
Type B	0	110	10	119 022
Type C	0	78	1	111 168

The substance/substance group *Uridine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9893 %)	91.6667 % (> 89.1667 %)
Type C	100.0000 % (> 99.8899 %)	98.7342 % (> 94.9367 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Uridine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Carmellose sodium (400 / 450 / 500 / 6...	39.21	—
Aciclovir	39.96	—
Trometamol	42.66	—
SyrSpend® SF Alka	45.65	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Uridine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
20744	20744	0.00	41.17
21895	20744	2.94	41.72
23529	20744	4.54	43.09

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Valine**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20405-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Valine; Valinum

Special notes

When selecting the *Valine* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Valine	5	7	6

Second-stage model

For differentiation of the substance/substance group *Valine* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Valine*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Valine	1604055	22571	40	20160601*
Euro OTC	Valine	1701026	23131	40	20170222*
Euro OTC	Valine	1904006	24611	40	20190423*
Euro OTC	Valine	1909028	24971	40	20191015*
Fagron	Valine	15A14-B07-307756	21953	60	9198

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 220 spectra of 5 reference samples from the substance/substance group *Valine*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 469 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 280 spectra of 7 reference samples from the substance/substance group *Valine*.
- Among them are spectra of independent samples from 7 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Valine	1609009	22799	40
Euro OTC	Valine	1705017	23426	40
Euro OTC	Valine	1710003	23770	40
Euro OTC	Valine	1712005	23867	40
Euro OTC	Valine	1803017	24091	40
Euro OTC	Valine	1805014	24119	40
Euro OTC	Valine	1809027	24304	40

- 118 862 spectra from a total of 2413 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 8 spectra from 7 *Apo-Ident* customers from 6 batches from the substance/substance group *Valine*.
- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Euro OTC	Valine	1604055-01	2
Euro OTC	Valine	1805014-02	2
Euro OTC	Valine	1710003-01	1
Euro OTC	Valine	L1309029-02	1
Fagron	Valine	121259	1
Fagron	Valine	13B13-N05	1

- 111 239 spectra from 742 *Apo-Ident* customers from a total of 31 885 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Valine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Valine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	220	0	110 469
Type B	0	280	0	118 862
Type C	0	7	1	111 239

The substance/substance group *Valine* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.8571 %)
Type C	100.0000 % (> 99.8900 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Valine* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levocarnitine	43.64	—
Isoleucine	44.45	—
L-leucine	47.96	—
Mometasone furoate, micronized	54.94	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Valine* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21953	21953	0.00	70.16
22571	22571	0.00	70.62
23131	23131	0.00	72.70
24971	24971	0.00	69.84
24611	24611	0.00	68.25

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Vancomycin hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 21748-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vancomycin hydrochloride; Vancomycini hydrochloridum

Special notes

When selecting the *Vancomycin hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vancomycin hydrochloride	8	3	0

Second-stage model

For differentiation of the substance/substance group *Vancomycin hydrochloride* the following second-stage model is used:

- [Submodel 9](#)

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vancomycin hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Audor Pharma	Vancomycin hydro...	APHAP1609006EV	23532	40	AR-18-FG-000670-01
Euro OTC	Vancomycin hydro...	1407047-01	21748	60	AR-15-FG-008950-01
Euro OTC	Vancomycin hydro...	1506029	21826	60	AR-15-FG-009077-01
Euro OTC	Vancomycin hydro...	1610038	22878	40	20161208*
Euro OTC	Vancomycin hydro...	1810013	24325	40	20181029*
Euro OTC	Vancomycin hydro...	1908025	24854	40	20190923*
Fagron	Vancomycin hydro...	17I18-B08-340944	24010	40	20171109
Fagron	Vancomycin hydro...	18L18-B02-359948	24696	40	20190207

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 360 spectra of 8 reference samples from the substance/substance group *Vancomycin hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 8 different batches.
- 110 329 spectra from a total of 1958 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 7 reference samples from the substance/substance group *Vancomycin hydrochloride*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Euro OTC	Vancomycin hydrochloride	1604037	22891	40
Euro OTC	Vancomycin hydrochloride	1812005	24421	40
Euro OTC	Vancomycin hydrochloride	1902014	24492	40
Euro OTC	Vancomycin hydrochloride	1407047-01	21748SI [†]	60
Euro OTC	Vancomycin hydrochloride	1506029	21826SI [†]	60
Euro OTC	Vancomycin hydrochloride	1610038	22878SI [†]	40
Euro OTC	Vancomycin hydrochloride	1604037	22891SI	40

- 118 822 spectra from a total of 2414 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 0 spectra from 0 *Apo-Ident* customers from 0 batches from the substance/substance group *Vancomycin hydrochloride*.
- Among them are spectra of independent samples from 0 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.
- 111 247 spectra from 742 *Apo-Ident* customers from a total of 31 891 batches from a further 707 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Vancomycin hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vancomycin hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	360	0	110 329
Type B	0	319	1	118 822
Type C	0	0	0	111 247

The substance/substance group *Vancomycin hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.3333 %)
Type B	100.0000 % (> 99.9893 %)	99.6875 % (> 98.7500 %)
Type C	100.0000 % (> 99.8902 %)	n/a (n/a)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vancomycin hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Levothyroxin sodium	17.84	51.23
Sodium cromoglicate	32.82	—
Hydrochlorothiazide	40.35	—
Sodium tetraborate	44.05	—
Oxytetracycline hydrochloride	45.64	—
Tosylchloramide sodium	49.07	—
Magnesium citrate	63.57	—
⋮	⋮	⋮
Ethacridine lactate monohydrate	>50	116.76
Chlortetracycline hydrochloride	>50	224.20

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vancomycin hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21748	21748	0.00	28.43
24854	24854	0.00	29.06
24325	24325	0.00	19.85
23532	23532	0.00	24.97
24010	23532	12.02	20.50
24696	21748	10.49	28.44
21826	21826	0.00	20.24
22878	22878	0.00	17.55

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Vanillin**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20204-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Vanillin; Vanillinum

Special notes

When selecting the *Vanillin* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vanillin	5	3	40

Second-stage model

For differentiation of the substance/substance group *Vanillin* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Vanillin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Vanillin	14044413	21737	60	20140227
Caelo	Vanillin	15135302	21924	60	AR-17-FG-022168-03
Caelo	Vanillin	160895	22484	60	20160421*
Caelo	Vanillin	191201	24719	40	20190515*
Fagron	Vanillin	13J01-N07	21738	60	20130926

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 5 reference samples from the substance/substance group *Vanillin*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 5 different batches.
- 110 409 spectra from a total of 1961 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Vanillin*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Vanillin	171172	23308	40
Caelo	Vanillin	17117201	23561	40
Caelo	Vanillin	173088	23805	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 101 spectra from 77 *Apo-Ident* customers from 43 batches from the substance/substance group *Vanillin*.
- Among them are spectra of independent samples from 40 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag	Vanillin	12H09-N06	1
Anzag	Vanillin	16089508	1
Caelo	Vanillin	10066830	1
Caelo	Vanillin	90961269	1
Caelo	Vanillin	12079407	2
Caelo	Vanillin	12079424	2
Caelo	Vanillin	12071401	1
Caelo	Vanillin	12079428	1
Caelo	Vanillin	15154006	1
Caelo	Vanillin	14044419	2
Caelo	Vanillin	15154020	6
Caelo	Vanillin	16089506	9
Caelo	Vanillin	17117201	1
Caelo	Vanillin	17117207	8
Caelo	Vanillin	18073507	3
Caelo	Vanillin	1089501	1
Caelo	Vanillin	10066811	1
Caelo	Vanillin	12079417	1
Caelo	Vanillin	15154014	3
Caelo	Vanillin	18073501	5
Caelo	Vanillin	112901	1
Caelo	Vanillin	18073506	1
Caelo	Vanillin	15227317	1
Caelo	Vanillin	16089508	3
Caelo	Vanillin	12079410	1
Caelo	Vanillin	18073509	1
Caelo	Vanillin	15154017	1
Caelo	Vanillin	12079412	2
Caelo	Vanillin	1514006	1
Caesar & Loretz GmbH D-...	Vanillin	10066830	1
Caesar & Loretz GmbH, 4...	Vanillin	12079401	1
Caesar & Loretz GmbH, 4...	Vanillin	12079412	1
Dr.Hollborn	Vanillin	6082015	1
Fagron	Vanillin	232050-0004	1
Fagron	Vanillin	12H09-N06	2

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Supplier	Substance	Batch	Spectra
Fagron	Vanillin	14G02-B99-296988	1
Fagron	Vanillin	11G28-N09	1
Fagron	Vanillin	8L05-N07	1
Fagron	Vanillin	314Q2548	1
Fagron	Vanillin	18073501	1
fargron	Vanillin	13/01-N07	1
Finteler Apotheke	Vanillin	17117201	1
Gatt-Koller	Vanillin	201770800	1
Gehe	Vanillin	12079412	1
Gehe	Vanillin	16089506	1
Gehe/Noweda	Vanillin	15154006	1
Hedinger/Ebert	Vanillin	13A30-N10	1
Jenne	Vanillin	18073501	1
Klosterring	Vanillin	17117207	1
L10	Vanillin	18073506	1
Caelo	Vanillin	16089501	3
L12	Vanillin	16089508	1
L12	Vanillin	17117201	1
L12	Vanillin	18073501	1
Rhodia GmbH/Noweda	Vanillin	12D02-N03	1
Sanacorp	Vanillin	12H09-N06	1
Caelo	Vanillin		1
Caelo	Vanillin	15135302	1
Fagron	Vanillin	13J01-N07	6

- 111 146 spectra from 742 *Apo-Ident* customers from a total of 31 850 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Vanillin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vanillin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	120	0	119 022
Type C	0	100	1	111 146

The substance/substance group *Vanillin* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	99.0099 % (> 96.0396 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several

new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Vanillin* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Paracetamol	19.23	—
Sodium cromoglicate	34.82	—
Serine	44.78	—
Griffonia seed extract	48.18	—
Sulfogaiacol hydrate	48.79	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vanillin* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
24719	24719	0.00	30.23
21737	22484	2.22	26.57
21738	22484	2.14	26.49
21924	21924	0.00	26.35
22484	22484	0.00	26.67

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Waxes / Fats**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20865-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Waxes / Fats; Adeps solidus; Adeps solidus W35; Cera alba; Cera flava; Cetyl palmitate 15; Cetyl palmitas 15; Cocoa butter; Hard fat in pastilles; Hard fat W35; Microcrystalline wax; Natrii laurylsulfuricum; Oleum cacao; Paraffin, hard; Paraffin, microcrystalline; Paraffinum durum in rotulis; Paraffinum microcrystallinum; Sodium dodecyl sulfate; Sodium dodecyl sulphate; Wax, bleached; Wax, yellow

Special notes

When selecting the *Waxes / Fats* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]

Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]

AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Cetyl palmitate 15	8	3	83
Cocoa butter	5	3	85

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Substance	Type A	Type B	Type C
Hard fat in pastilles	4	5	106
Hard fat W35	4	2	25
Paraffin, hard	2	1	61
Paraffin, microcrystalline	3	1	17
Sodium dodecyl sulfate	6	5	37
Wax, bleached	3	3	60
Wax, yellow	4	2	241

Second-stage model

For differentiation of the substance/substance group *Waxes / Fats* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Waxes / Fats*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Cetyl palmitate 15	12331916	20865	40	1402429
Caelo	Cetyl palmitate 15	14351606	21875	60	20141219
Caelo	Cetyl palmitate 15	15301703	21984	60	AR-16-FG-007435-01
Caelo	Cetyl palmitate 15	15301703	22325	60	20151013
Caelo	Cetyl palmitate 15	160538	22486	60	20160323*
Caelo	Cetyl palmitate 15	17043503	23560	40	20170306
Caelo	Cetyl palmitate 15	171640	23639	40	20170719*
Caelo	Cetyl palmitate 15	172715	23817	40	20171124*
Caelo	Cetyl palmitate 15	191390	24720	40	20190702*
Caelo	Cocoa butter	13292013	21482	40	20130924
Caelo	Cocoa butter	14348906	22348	60	20150122
Caelo	Cocoa butter	163165	23067	40	20161116*
Caelo	Cocoa butter	17055907	23707	33	20170310
Caelo	Cocoa butter	190360	24813	40	20190227*
Bombastus	Hard fat in past...	306363	23565	34	20161213
Bombastus	Hard fat in past...	308558	23705	40	20170321
Caelo	Hard fat in past...	12158122	21067	40	20120627
Caelo	Hard fat in past...	160278	22479	60	20160407*
Fagron	Hard fat W35	15A07-B12-302751	21880	60	1604639
Fagron	Hard fat W35	15A07-B12-309245	22338	60	20150115
Fagron	Hard fat W35	16K08-B10-334910	23601	40	20161229
Fagron	Hard fat W35	19C04-B09-191420	25047	40	20190330
Caelo	Paraffin, hard	13390413	21731	60	20131213
Caelo	Paraffin, hard	15232004	22349	60	1702507
Caelo	Paraffin, microc...	14307104	21682	60	AR-15-FG-005277-01
Caelo	Paraffin, microc...	14307106	21766	60	20141014
Caelo	Paraffin, microc...	154128	22330	60	20160112*
Caelo	Sodium dodecyl s...	13099011	20986	40	1403108
Caelo	Sodium dodecyl s...	15344503	22352	60	20151022
Caelo	Sodium dodecyl s...	16229217	23242	40	20160809
Caelo	Sodium dodecyl s...	170955	23278	40	20170503*
Caelo	Sodium dodecyl s...	191243	24715	40	20190521*
Caelo	Sodium dodecyl s...	190923	24716	40	20190521*
Caelo	Wax, bleached	13378619	21483	20	1509364
Caelo	Wax, bleached	14336620	22244	60	20141125

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Wax, bleached	15292022	22956	40	20150827
Caelo	Wax, yellow	13335507	21433	60	20131011
Caelo	Wax, yellow	15317602	22245	60	20151007
Klenk	Wax, yellow	0290A170314	23511	40	1908177
Klenk	Wax, yellow	0290A170915	24870	40	20190507

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 1907 spectra of 40 reference samples from the substance/substance group *Waxes / Fats*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 39 different batches.
- 108 782 spectra from a total of 1927 batches from further 382 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1053 spectra of 28 reference samples from the substance/substance group *Waxes / Fats*.
- Among them are spectra of independent samples from 25 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Cetyl palmitate 15	13295919	21316	20
Caelo	Cetyl palmitate 15	181499	24221	40
Caelo	Cetyl palmitate 15	182737	24356	40
Caelo	Cocoa butter	173149	23795	40
Caelo	Cocoa butter	181351	24226	40
Caelo	Cocoa butter	182544	24363	40
Bombastus	Hard fat in pastilles	18006248	24663	40
Caelo	Hard fat in pastilles	173076	23814	40

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*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

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Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Hard fat in pastilles	181479	24228	40
Caelo	Hard fat in pastilles	183339	24529	40
Caelo	Hard fat in pastilles	191940	24887	40
Fagron	Hard fat W35	15J08-B04-324959	22806	40
Fagron	Hard fat W35	17K09-B03-343779	24114	40
Caelo	Paraffin, hard	16277704	23190	40
Caelo	Paraffin, microcrystalline	15412801	23724	40
Caelo	Sodium dodecyl sulfate	13411305	21465	60
Caelo	Sodium dodecyl sulfate	16229205	23243	40
Caelo	Sodium dodecyl sulfate	172363	23664	40
Caelo	Sodium dodecyl sulfate	181822	24292	40
Caelo	Sodium dodecyl sulfate	190187	24549	40
Caelo	Wax, bleached	161631	22587	40
Caelo	Wax, bleached	16163109	23513	40
Caelo	Wax, bleached	182391	24351	40
Caelo	Wax, yellow	162750	22767	40
Caelo	Wax, yellow	17011602	23512	40
Caelo	Cetyl palmitate 15	13295919	21522	40
Caelo	Cocoa butter	17055907	23707 [†]	7
Bombastus	Hard fat in pastilles	306363	23565 [†]	6

- 118 089 spectra from a total of 2393 batches from further 791 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 2706 spectra from 485 *Apo-Ident* customers from 709 batches from the substance/substance group *Waxes / Fats*.
- Among them are spectra of independent samples from 679 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Cetyl palmitate 15	15301709	5
Alliance H.	Cetyl palmitate 15	15301709	1
Alliance Healthcare	Cetyl palmitate 15	13131905	1
Anzag	Cetyl palmitate 15	12018208	1
Caelo	Cetyl palmitate 15	14060709	6
Caelo	Cetyl palmitate 15	26071201	1
Caelo	Cetyl palmitate 15	12082901	1
Caelo	Cetyl palmitate 15	12018208	6
Caelo	Cetyl palmitate 15	11042019	1
Caelo	Cetyl palmitate 15	12228808	3
Caelo	Cetyl palmitate 15	1228808	1
Caelo	Cetyl palmitate 15	12018204/Int212191	1
Caelo	Cetyl palmitate 15	12228801/Int212191	1
Caelo	Cetyl palmitate 15	30101301	1

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[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

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Supplier	Substance	Batch	Spectra
Caelo	Cetyl palmitate 15	13131914	4
Caelo	Cetyl palmitate 15	13295921	1
Caelo	Cetyl palmitate 15	11021502	1
Caelo	Cetyl palmitate 15	14041505	1
Caelo	Cetyl palmitate 15	14351602	5
Caelo	Cetyl palmitate 15	14351601	2
Caelo	Cetyl palmitate 15	14213706	1
Caelo	Cetyl palmitate 15	13131905NP	1
Caelo	Cetyl palmitate 15	15301701	7
Caelo	Cetyl palmitate 15	15632	1
Caelo	Cetyl palmitate 15	15301705	8
Caelo	Cetyl palmitate 15	16053803	9
Caelo	Cetyl palmitate 15	15301708	1
Caelo	Cetyl palmitate 15	16053804	1
Caelo	Cetyl palmitate 15	16053811	7
Caelo	Cetyl palmitate 15	16186805	17
Caelo	Cetyl palmitate 15	28041731	1
Caelo	Cetyl palmitate 15	17043504	10
Caelo	Cetyl palmitate 15	17164005	16
Caelo	Cetyl palmitate 15	18149902	1
Caelo	Cetyl palmitate 15	19121803	1
Caelo	Cetyl palmitate 15	19139004	6
Caelo	Cetyl palmitate 15	17271504	7
Caelo	Cetyl palmitate 15	12228805	1
Caelo	Cetyl palmitate 15	14351609	3
Caelo	Cetyl palmitate 15	14351614	1
Caelo	Cetyl palmitate 15	12228818	5
Caelo	Cetyl palmitate 15	18149912	5
Caelo	Cetyl palmitate 15	12331919	2
Caelo	Cetyl palmitate 15	13131905	3
Caelo	Cetyl palmitate 15	13295919	10
Caelo	Cetyl palmitate 15	17164007	1
Caelo	Cetyl palmitate 15	12018215	1
Caelo	Cetyl palmitate 15	13295910	8
Caelo	Cetyl palmitate 15	14060705	6
Caelo	Cetyl palmitate 15	14213705	3
Caelo	Cetyl palmitate 15	142137710	1
Caelo	Cetyl palmitate 15	14351607	1
Caelo	Cetyl palmitate 15	16053805	2
Caelo	Cetyl palmitate 15	18273704	6
Caelo	Cetyl palmitate 15	14060706	6
Caelo	Cetyl palmitate 15	12018204	3
Caelo	Cetyl palmitate 15	16186806	1
Caelo	Cetyl palmitate 15	17164004	12
Caelo	Cetyl palmitate 15	17043509	1
Caelo	Cetyl palmitate 15	17271506	1
Caelo	Cetyl palmitate 15	10068410	1
Caelo	Cetyl palmitate 15	14213710	2
Caelo	Cetyl palmitate 15	14213709	4
Caelo	Cetyl palmitate 15	17271502	5
Caelo	Cetyl palmitate 15	17271505	8
Caelo	Cetyl palmitate 15	18149904	9
Caelo	Cetyl palmitate 15	13131906	7
Caelo	Cetyl palmitate 15	1313190	1
Caelo	Cetyl palmitate 15	14351612	14
Caelo	Cetyl palmitate 15	15301711	7
Caesar & Lorenz GmbH	Cetyl palmitate 15	17043504	1
Caesar & Loretz GmbH	Cetyl palmitate 15	10068402	2
Caesar & Loretz GmbH	Cetyl palmitate 15	16186805	1
Caesar & Loretz GmbH	Cetyl palmitate 15	17164005	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Cetyl palmitate 15	18149912	1
Caesar & Loretz GmbH	Cetyl palmitate 15	18273704	2
Caesar & Loretz GmbH / ...	Cetyl palmitate 15	17271505	1
Caesar & Loretz GmbH / ...	Cetyl palmitate 15	18149912	1
Caesar u Loretz	Cetyl palmitate 15	14213710	1
Caesar/Noweda	Cetyl palmitate 15	12228801	1
Caesar/Noweda	Cetyl palmitate 15	13295909	1
Caesar/Noweda	Cetyl palmitate 15	15301701	1
Caesar & Loretz GmbH / ...	Cetyl palmitate 15	18149904	1
coelo/Sana	Cetyl palmitate 15	14351612	1
Euro OTC	Cetyl palmitate 15	160419C	1
Fagron	Cetyl palmitate 15	12D19-N02	1
Fagron	Cetyl palmitate 15	17164005	1
Fagron	Cetyl palmitate 15	12C27-N07	2
Fagron	Cetyl palmitate 15	18149904	1
Fagron/Alliance HC	Cetyl palmitate 15	14351612	1
Fischer/Phönix	Cetyl palmitate 15	15301711	1
Gehe	Cetyl palmitate 15	8209646	1
Caelo	Cetyl palmitate 15	13131911	2
Caelo	Cetyl palmitate 15	16186809	13
L10	Cetyl palmitate 15	16053811	1
L10	Cetyl palmitate 15	16186805	1
L12	Cetyl palmitate 15	18149904	2
L30	Cetyl palmitate 15	17271505	1
Nachprüfung	Cetyl palmitate 15	3012U01241	1
Nachprüfung	Cetyl palmitate 15	4917I-01242	1
Euro OTC	Cetyl palmitate 15	12228808	1
Phoenix	Cetyl palmitate 15	14060705	1
Phoenix	Cetyl palmitate 15	17164005	1
Phoenix	Cetyl palmitate 15	18149912	1
Caelo	Cetyl palmitate 15	15301704	5
Phönix	Cetyl palmitate 15	13131906	1
Phönix	Cetyl palmitate 15	13295919	1
Sanacorp	Cetyl palmitate 15	8/AKD12	1
Sanacorp	Cetyl palmitate 15	8/AKD13	1
Sanacorp	Cetyl palmitate 15	16186805	1
ACM	Cocoa butter	KNC1605J15	1
AHD	Cocoa butter	14348906	1
Anzag	Cocoa butter	11117816	1
Anzag	Cocoa butter	12342004	1
Bombastus	Cocoa butter	17314901	1
Caelo	Cocoa butter	13140407	3
Caelo	Cocoa butter	13140406	3
Caelo	Cocoa butter	103276705	1
Caelo	Cocoa butter	12040803	1
Caelo	Cocoa butter	11034719	1
Caelo	Cocoa butter	12040802	1
Caelo	Cocoa butter	11117816	1
Caelo	Cocoa butter	12040807	2
Caelo	Cocoa butter	12270202	4
Caelo	Cocoa butter	12342003	7
Caelo	Cocoa butter	12270203	4
Caelo	Cocoa butter	12342004	2
Caelo	Cocoa butter	13027202	4
Caelo	Cocoa butter	13027203	1
Caelo	Cocoa butter	13027207	1
Caelo	Cocoa butter	13027221	4
Caelo	Cocoa butter	12270210	2
Caelo	Cocoa butter	13027224	5
Caelo	Cocoa butter	13140401	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Cocoa butter	13140404	2
Caelo	Cocoa butter	13292007	9
Caelo	Cocoa butter	13292001	2
Caelo	Cocoa butter	13292012	3
Caelo	Cocoa butter	14123611	6
Caelo	Cocoa butter	13140409	1
Caelo	Cocoa butter	14045104	1
Caelo	Cocoa butter	14123609	2
Caelo	Cocoa butter	14304703	1
Caelo	Cocoa butter	14123620	6
Caelo	Cocoa butter	14123621	1
Caelo	Cocoa butter	15088904	1
Caelo	Cocoa butter	515A-03176	1
Caelo	Cocoa butter	14348909	2
Caelo	Cocoa butter	16049201	3
Caelo	Cocoa butter	16062604	1
Caelo	Cocoa butter	17055905	1
Caelo	Cocoa butter	17055908	5
Caelo	Cocoa butter	17055913	1
Caelo	Cocoa butter	17314902	20
Caelo	Cocoa butter	18135101	1
Caelo	Cocoa butter	18135107	1
Caelo	Cocoa butter	18135112	4
Caelo	Cocoa butter	18254412	3
Caelo	Cocoa butter	11034718	1
Caelo	Cocoa butter	17055902	10
Caelo	Cocoa butter	18135106	2
Caelo	Cocoa butter	18135102	3
Caelo	Cocoa butter	170555901	1
Caelo	Cocoa butter	17314901	4
Caelo	Cocoa butter	15088903	1
Caelo	Cocoa butter	16316508	22
Caelo	Cocoa butter	18254402	1
Caelo	Cocoa butter	13292011	2
Caelo	Cocoa butter	19036008	1
Caelo	Cocoa butter	15088905	1
Caelo	Cocoa butter	16062602	1
Caelo	Cocoa butter	16316501	4
Caelo	Cocoa butter	163116508	1
Caelo	Cocoa butter	16049209	2
Caelo	Cocoa butter	16316509	5
Caelo	Cocoa butter	12270201	2
Caelo	Cocoa butter	14348908	2
Caelo	Cocoa butter	13027204	4
Caelo	Cocoa butter	13140405	3
Caelo	Cocoa butter	15246102	4
Caelo	Cocoa butter	12270209	2
Caelo	Cocoa butter	14123617	4
Caelo	Cocoa butter	1392013	1
Caelo	Cocoa butter	13292019	3
Caelo	Cocoa butter	13027227	3
Caelo	Cocoa butter	13292006	4
Caesar & Lorenz	Cocoa butter	13140404	1
Caesar & Loretz GmbH	Cocoa butter	12270210	2
Caesar & Loretz GmbH	Cocoa butter	18135106	1
Caesar & Loretz GmbH	Cocoa butter	19036007	2
Caesar & Loretz GmbH / ...	Cocoa butter	16316503	1
Caesar & Loretz GmbH / ...	Cocoa butter	17055908	1
Caesar & Loretz GmbH / ...	Cocoa butter	16316509	1
Caesar & Loretz GmbH/Fi...	Cocoa butter	18254402	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Cealo / Noweda	Cocoa butter	13292011	1
Euro OTC	Cocoa butter	14123621	1
Euro OTC	Cocoa butter	16316508	1
Gatt-Koller	Cocoa butter	1803838	1
Gutenberg-Apotheke	Cocoa butter	13292007	1
Cealo	Cocoa butter	13027226	4
Cealo	Cocoa butter	13292015	1
L12	Cocoa butter	16316508	1
Cealo	Cocoa butter	16316503	6
Noweda	Cocoa butter	11117813	2
Phönix	Cocoa butter	27121	1
sanacorp	Cocoa butter	13140407	1
Sanacorp	Cocoa butter	13027207	1
Sanacorp	Cocoa butter	AKD27	1
Sanacorp	Cocoa butter	AKD28	1
Sanacorp	Cocoa butter	17055908	3
Sanacorp	Cocoa butter	170559908	1
Sanacorp	Cocoa butter	17314902	1
Sanacorp	Cocoa butter	18135106	3
spinnrad	Cocoa butter	3252	1
Spinnrad	Cocoa butter	512300202	1
Spinnrad	Cocoa butter	1017300203	1
AHD	Hard fat in pastilles	277212	2
apomix	Hard fat in pastilles	18147901	1
Bombastus	Hard fat in pastilles	273759	1
Bombastus	Hard fat in pastilles	287287	1
Bombastus	Hard fat in pastilles	18004024	1
Bombastus	Hard fat in pastilles	293848	7
Bombastus	Hard fat in pastilles	302709	3
Bombastus	Hard fat in pastilles	18000346	5
Bombastus	Hard fat in pastilles	308559	2
Bombastus	Hard fat in pastilles	17107304	2
Cae4lo	Hard fat in pastilles	15185002	1
Cealo	Hard fat in pastilles	17107304	5
Cealo	Hard fat in pastilles	11109623	2
Cealo	Hard fat in pastilles	11109617	1
Cealo	Hard fat in pastilles	11345905	3
Cealo	Hard fat in pastilles	12111204	1
Cealo	Hard fat in pastilles	11345918	7
Cealo	Hard fat in pastilles	24011302	1
Cealo	Hard fat in pastilles	11345904	1
Cealo	Hard fat in pastilles	12158104	5
Cealo	Hard fat in pastilles	12158115	6
Cealo	Hard fat in pastilles	7101304	1
Cealo	Hard fat in pastilles	13243403	8
Cealo	Hard fat in pastilles	13243416	1
Cealo	Hard fat in pastilles	13243414	1
Cealo	Hard fat in pastilles	13243411	3
Cealo	Hard fat in pastilles	14126203	7
Cealo	Hard fat in pastilles	13243412	2
Cealo	Hard fat in pastilles	13243420	1
Cealo	Hard fat in pastilles	17041401	1
Cealo	Hard fat in pastilles	13243419	3
Cealo	Hard fat in pastilles	14126205	1
Cealo	Hard fat in pastilles	14126204	2
Cealo	Hard fat in pastilles	1412602	1
Cealo	Hard fat in pastilles	15111402	1
Cealo	Hard fat in pastilles	14126210	3
Cealo	Hard fat in pastilles	14126216	2
Cealo	Hard fat in pastilles	14126217	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Hard fat in pastilles	16021503	1
Caelo	Hard fat in pastilles	14338703	3
Caelo	Hard fat in pastilles	14338707	3
Caelo	Hard fat in pastilles	14338711	2
Caelo	Hard fat in pastilles	20071501	1
Caelo	Hard fat in pastilles	14338708	1
Caelo	Hard fat in pastilles	15185003	11
Caelo	Hard fat in pastilles	15185009	10
Caelo	Hard fat in pastilles	1518505	1
Caelo	Hard fat in pastilles	15185007	2
Caelo	Hard fat in pastilles	16027801	5
Caelo	Hard fat in pastilles	16027805	4
Caelo	Hard fat in pastilles	16027806	1
Caelo	Hard fat in pastilles	16274205	3
Caelo	Hard fat in pastilles	8041710	1
Caelo	Hard fat in pastilles	16274208	13
Caelo	Hard fat in pastilles	17107301	7
Caelo	Hard fat in pastilles	27101703	1
Caelo	Hard fat in pastilles	17107306	2
Caelo	Hard fat in pastilles	17307601	23
Caelo	Hard fat in pastilles	8051810	1
Caelo	Hard fat in pastilles	17307604	1
Caelo	Hard fat in pastilles	29061803	1
Caelo	Hard fat in pastilles	18040401	10
Caelo	Hard fat in pastilles	17307607	1
Caelo	Hard fat in pastilles	18147902	14
Caelo	Hard fat in pastilles	18333904	7
Caelo	Hard fat in pastilles	170921AS/16274208	1
Caelo	Hard fat in pastilles	16274203	11
Caelo	Hard fat in pastilles	17307602	5
Caelo	Hard fat in pastilles	18147901	4
Caelo	Hard fat in pastilles	18147908	2
Caelo	Hard fat in pastilles	12158119	1
Caelo	Hard fat in pastilles	14338704	4
Caelo	Hard fat in pastilles	18333905	1
Caelo	Hard fat in pastilles	13243301	5
Caelo	Hard fat in pastilles	14338705	1
Caelo	Hard fat in pastilles	14126202	5
Caelo	Hard fat in pastilles	14338706	1
Caelo	Hard fat in pastilles	12158109	3
Caelo	Hard fat in pastilles	12158114	3
Caelo	Hard fat in pastilles	13243409	5
Caelo	Hard fat in pastilles	13243418	3
Caelo	Hard fat in pastilles	14126218	2
Caelo	Hard fat in pastilles	15185002	14
Caelo	Hard fat in pastilles	15185005	12
Caelo	Hard fat in pastilles	16027802	7
Caelo	Hard fat in pastilles	90915429	1
Caelo	Hard fat in pastilles	16274201	13
Caelo	Hard fat in pastilles	16274202	1
Caesar & Loretz GmbH	Hard fat in pastilles	18333903	2
Caesar & Loretz GmbH	Hard fat in pastilles	18040401	1
Caesar & Loretz GmbH D-...	Hard fat in pastilles	12158104	1
Caesar & Loretz GmbH, 4...	Hard fat in pastilles	11345918	1
Caesar & Loretz GmbH, 4...	Hard fat in pastilles	13243403	1
Caesar & Loretz GmbH/ F...	Hard fat in pastilles	18147908	1
Caesar & Loretz GmbH/E	Hard fat in pastilles	18333904	1
Caesar & Loretz GmbH/Fi...	Hard fat in pastilles	18333904	1
Caesar & Loretz GmbH/Fi...	Hard fat in pastilles	18333905	1
Caesar Loretz GmbH	Hard fat in pastilles	17307602	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar&Loretz GmbH D-40...	Hard fat in pastilles	11109617	1
Caesar/Noweda	Hard fat in pastilles	14126203	1
Caesar und Loretz GmbH	Hard fat in pastilles	18333905	1
China Medica	Hard fat in pastilles	3244303	1
Euro OTC	Hard fat in pastilles	17107304	1
Euro OTC	Hard fat in pastilles	15185005	1
Fagron	Hard fat in pastilles	12I04-N11	1
Fagron	Hard fat in pastilles	12K01-N12	3
Fagron	Hard fat in pastilles	15F03-B06	4
Fagron	Hard fat in pastilles	12158115	2
Fagron	Hard fat in pastilles	13D10-N06	1
Fagron	Hard fat in pastilles	12G04-N18	1
Fagron	Hard fat in pastilles	14G03-B03-296731	1
Fagron	Hard fat in pastilles	14L01-B06	2
Fagron	Hard fat in pastilles	15F03-B06-308708	3
Fagron	Hard fat in pastilles	13243301	1
Fagron	Hard fat in pastilles	14L01-B06-303380	3
Fagron	Hard fat in pastilles	606469	1
Fagron	Hard fat in pastilles	16H01-B03-334976	1
Fargon	Hard fat in pastilles	41319264	1
Gehe	Hard fat in pastilles	11345918	1
Gehe	Hard fat in pastilles	13243403	1
GEHE	Hard fat in pastilles	16274203	1
GEHE	Hard fat in pastilles	18147901	2
Caelo	Hard fat in pastilles	10158813	1
Caelo	Hard fat in pastilles	1135917	1
Caelo	Hard fat in pastilles	11345917	3
Nachprüfung vom 31.01.2...	Hard fat in pastilles	15185002	1
Noweda	Hard fat in pastilles	11345909	1
Phoenix	Hard fat in pastilles	18333904	1
Phoenix 3.3.14	Hard fat in pastilles	13243414	1
Phönix	Hard fat in pastilles	277212	1
Phönix	Hard fat in pastilles	16274203	1
Phönix	Hard fat in pastilles	18000346	1
Phönix	Hard fat in pastilles	18147902	2
Phytocomm	Hard fat in pastilles	209314	1
Purren Apotheke	Hard fat in pastilles	10I03-N08	1
Rondell Apotheke	Hard fat in pastilles	15185002	1
sanacorp	Hard fat in pastilles	14338703	1
Sanacorp	Hard fat in pastilles	14126203	1
Sanacorp	Hard fat in pastilles	16274202	1
Caelo	Hard fat W35	16271201	1
Caelo	Hard fat W35	16K08-B10	1
Caelo	Hard fat W35	18333906	1
Caelo	Hard fat W35	18G13-B02-356977	1
Caesar & Loretz GmbH	Hard fat W35	17307601	1
Euro OTC	Hard fat W35	17K09B03343780	1
Fagron	Hard fat W35	15J08-B04-324217	1
Fagron	Hard fat W35	15J08-B04-324959	2
Fagron	Hard fat W35	16K08-B10-332763	2
Fagron	Hard fat W35	15J08-B04-322727	1
Fagron	Hard fat W35	17K09-B03-346709	1
Fagron	Hard fat W35	17k09-b03-351980	1
Fagron	Hard fat W35	18G13-B02-355398	1
Fagron	Hard fat W35	18G13-B02	1
Fagron	Hard fat W35	16K08-B10-339077	4
Fagron	Hard fat W35	17K09-B03-351980	3
Fagron	Hard fat W35	17K09-B03-348770	3
Fagron	Hard fat W35	18G13-B02-356977	1
Fagron	Hard fat W35	15J08-B04-322726	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Hard fat W35	3914E-02328	1
Kehr	Hard fat W35	17K09-B03-351980	1
Noweda	Hard fat W35	16027801	1
Phoenix	Hard fat W35	16k08-b10-332763	1
Phoenix	Hard fat W35	3076	1
Caelo	Paraffin, hard	12252211	3
Caelo	Paraffin, hard	12252221	3
Caelo	Paraffin, hard	11021202	1
Caelo	Paraffin, hard	13109221	1
Caelo	Paraffin, hard	13390415	3
Caelo	Paraffin, hard	14286503	1
Caelo	Paraffin, hard	14286511	2
Caelo	Paraffin, hard	13390408	1
Caelo	Paraffin, hard	1523002	1
Caelo	Paraffin, hard	15295406	3
Caelo	Paraffin, hard	15295407	2
Caelo	Paraffin, hard	16000903	3
Caelo	Paraffin, hard	16000910	1
Caelo	Paraffin, hard	16000922	3
Caelo	Paraffin, hard	16000921	3
Caelo	Paraffin, hard	16277706	6
Caelo	Paraffin, hard	18070131	7
Caelo	Paraffin, hard	12252206	1
Caelo	Paraffin, hard	302709	1
Caelo	Paraffin, hard	18070112	5
Caelo	Paraffin, hard	10194101	2
Caelo	Paraffin, hard	13109203	4
Caelo	Paraffin, hard	13390406	4
Caelo	Paraffin, hard	11363206	2
Caelo	Paraffin, hard	14286502	1
Caelo	Paraffin, hard	16000912	4
Caelo	Paraffin, hard	14286504	1
Caelo	Paraffin, hard	17245602	10
Caelo	Paraffin, hard	16277710	3
Caelo	Paraffin, hard	1136206	1
Caelo	Paraffin, hard	123654	1
Caelo	Paraffin, hard	13109224	4
Caelo	Paraffin, hard	12252205	2
Caelo	Paraffin, hard	13109218	1
Caelo	Paraffin, hard	13390403	1
Caelo	Paraffin, hard	14286517	4
Caelo	Paraffin, hard	15232001	1
Caelo	Paraffin, hard	11363205	1
Caelo	Paraffin, hard	13109213	6
Caelo	Paraffin, hard	152320004	1
Caelo	Paraffin, hard	16277705	2
Caelo	Paraffin, hard	11363220	3
Caelo	Paraffin, hard	16277716	1
Caelo	Paraffin, hard	15295405	5
Caelo	Paraffin, hard	15295410	4
Caelo	Paraffin, hard	17245604	1
Caelo	Paraffin, hard	16277704	4
Caelo	Paraffin, hard	18070107	15
Caelo	Paraffin, hard	18070118	4
Caesar & Loretz	Paraffin, hard	18070107	1
Caesar & Loretz GmbH	Paraffin, hard	17347701	1
Caesar & Loretz GmbH	Paraffin, hard	18070131	1
Cealo/AHD	Paraffin, hard	15295411	2
Euro OTC	Paraffin, hard	13109224	1
Gehe	Paraffin, hard	15295410	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
GEHE	Paraffin, hard	15295409	1
Caelo	Paraffin, hard	15295414	3
HCK	Paraffin, hard	16277705	1
Jenne	Paraffin, hard	17347701	1
Kehr	Paraffin, hard	17347701	1
Caelo	Paraffin, hard	17347701	14
L30	Paraffin, hard	17347701	1
Noweda	Paraffin, hard	11363206	1
Noweda	Paraffin, hard	14286517	1
Phoenix	Paraffin, hard	15295410	1
Phoenix	Paraffin, hard	18070131	1
Phoenix goettingen 09.05	Paraffin, hard	13390415	1
Caelo	Paraffin, hard	13109214	4
Unisan	Paraffin, hard	11166911	3
Caelo	Paraffin, microcrystalline	52622395	1
Caelo	Paraffin, microcrystalline	3042012M1	1
Caelo	Paraffin, microcrystalline	30101202	1
Caelo	Paraffin, microcrystalline	7111201	1
Caelo	Paraffin, microcrystalline	7111202	1
Caelo	Paraffin, microcrystalline	13274301	1
Caelo	Paraffin, microcrystalline	17137502	1
Caelo	Paraffin, microcrystalline	13274303	5
Caelo	Paraffin, microcrystalline	12095101	1
Caelo	Paraffin, microcrystalline	12355001	1
Caelo	Paraffin, microcrystalline	15412801	2
Caelo	Paraffin, microcrystalline	15412808	1
Caelo	Paraffin, microcrystalline	14307110	1
Gehe	Paraffin, microcrystalline	17137508	1
Caelo	Paraffin, microcrystalline	14307108	2
L12	Paraffin, microcrystalline	17137502	1
Noweda	Paraffin, microcrystalline	12266304	1
Phönix	Paraffin, microcrystalline	13274301	1
Caelo	Paraffin, microcrystalline	16000911	5
Caelo	Sodium dodecyl sulfate	16229213	2
Caelo	Sodium dodecyl sulfate	12153010	3
Caelo	Sodium dodecyl sulfate	12153019	1
Caelo	Sodium dodecyl sulfate	13099006	3
Caelo	Sodium dodecyl sulfate	13411302	2
Caelo	Sodium dodecyl sulfate	13411304	1
Caelo	Sodium dodecyl sulfate	14127406	1
Caelo	Sodium dodecyl sulfate	14127411	1
Caelo	Sodium dodecyl sulfate	26031508	1
Caelo	Sodium dodecyl sulfate	15095404	1
Caelo	Sodium dodecyl sulfate	15119907	3
Caelo	Sodium dodecyl sulfate	15344505	2
Caelo	Sodium dodecyl sulfate	15344515	2
Caelo	Sodium dodecyl sulfate	16229209	1
Caelo	Sodium dodecyl sulfate	18045202	1
Caelo	Sodium dodecyl sulfate	18182206	3
Caelo	Sodium dodecyl sulfate	1812207	1
Caelo	Sodium dodecyl sulfate	11220208	1
Caelo	Sodium dodecyl sulfate	13014604	2
Caelo	Sodium dodecyl sulfate	14283904	3
Caelo	Sodium dodecyl sulfate	12153003	1
Caelo	Sodium dodecyl sulfate	16229206	4
Caelo	Sodium dodecyl sulfate	13411305	3
Caelo	Sodium dodecyl sulfate	15344510	5
Caelo	Sodium dodecyl sulfate	15344511	1
Caelo	Sodium dodecyl sulfate	16229205	3
Caelo	Sodium dodecyl sulfate	16229220	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sodium dodecyl sulfate	17095505	1
Caelo	Sodium dodecyl sulfate	12153004	1
Caelo	Sodium dodecyl sulfate	16229218	1
Caelo	Sodium dodecyl sulfate	17095504	4
Caesar & Loretz GmbH	Sodium dodecyl sulfate	17095504	1
Caesar & Loretz GmbH / ...	Sodium dodecyl sulfate	16229205	1
Fagron	Sodium dodecyl sulfate	16229205	1
Gehe	Sodium dodecyl sulfate	14127404	1
GEHE	Sodium dodecyl sulfate	16229205	1
Ichthyol/Phönix	Sodium dodecyl sulfate	15344510	1
Intern Drogen	Sodium dodecyl sulfate	216991080	1
Caelo	Sodium dodecyl sulfate	17095511	8
Caelo	Sodium dodecyl sulfate	14224206	1
Sanacorp	Sodium dodecyl sulfate	5/AKD1	1
Sanacorp	Sodium dodecyl sulfate	5/AKD6	1
Bombastus	Wax, bleached	16163109	1
Bombastus	Wax, bleached	280A171019	1
Caelo	Wax, bleached	280A150528	1
Caelo	Wax, bleached	151210CA	1
Caelo	Wax, bleached	16163101	1
Caelo	Wax, bleached	16163105	28
Caelo	Wax, bleached	16163109	14
Caelo	Wax, bleached	3051808	1
Caelo	Wax, bleached	29091805	1
Caelo	Wax, bleached	18239104	6
Caelo	Wax, bleached	15292002	1
Caelo	Wax, bleached	2271200	1
Caelo	Wax, bleached	16163106	1
Caelo	Wax, bleached	10651388	1
Caelo	Wax, bleached	15292015	1
Caelo	Wax, bleached	18048904	1
Caelo	Wax, bleached	18048901	27
Caelo	Wax, bleached	17091802	27
Caelo	Wax, bleached	18239107	1
Caelo	Wax, bleached	19124203	2
Caelo	Wax, bleached	19124202	7
Caelo	Wax, bleached	15292010	1
Caelo	Wax, bleached	15292011	1
Caelo	Wax, bleached	17091803	6
Caelo	Wax, bleached	19124208	1
Caelo	Wax, bleached	18239102	17
Caelo	Wax, bleached	18239106	11
Caelo	Wax, bleached	19124206	4
Caelo	Wax, bleached	280A171019	1
Caelo	Wax, bleached	18048903	4
Caelo	Wax, bleached	16163115	2
Caelo	Wax, bleached	18048907	5
Caelo	Wax, bleached	122570	1
Caesar & Loretz GmbH	Wax, bleached	16163105	1
Caesar & Loretz GmbH	Wax, bleached	18048901	1
Caesar & Loretz GmbH	Wax, bleached	18239104	2
Caesar & Loretz GmbH	Wax, bleached	18239102	2
Caesar & Loretz GmbH	Wax, bleached	18239106	1
Caesar & Loretz GmbH / ...	Wax, bleached	15292010	1
Caesar & Loretz GmbH / ...	Wax, bleached	16163115	3
Caesar & Loretz GmbH / ...	Wax, bleached	18048907	2
Euro OTC	Wax, bleached	16163104	1
Fagron	Wax, bleached	2155	1
Fagron	Wax, bleached	15292009	1
Fagron	Wax, bleached	1701947	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Wax, bleached	16A28-B10-322948	1
Fagron	Wax, bleached	17L04-B05-348865	3
Fagron	Wax, bleached	16a28_b10_322948	1
Fagron	Wax, bleached	17C15-B01-354806	1
Fagron	Wax, bleached	15292022	1
GEHE	Wax, bleached	16163109	1
Kehr	Wax, bleached	18048906	1
Klenk	Wax, bleached	280A160311	12
Klenk	Wax, bleached	280A190715	4
Noweda	Wax, bleached	16163114	1
Caelo	Wax, bleached	14336621	1
Pharmachem	Wax, bleached	15292014	1
Phoenix	Wax, bleached	15292003	1
Phoenix	Wax, bleached	16163109	1
Phoenix	Wax, bleached	19124206	1
Fagron	Wax, bleached	17C15-B01-342088	1
phönix	Wax, bleached	15292022	1
phönix	Wax, bleached	16163109	1
Caelo	Wax, bleached	1529003	1
Sanacorp	Wax, bleached	16163114	1
Spinnrad	Wax, bleached	317048061	1
Spinnrad	Wax, bleached	118048061	1
Spinnrad	Wax, bleached	1018048062	1
AHD	Wax, yellow	15022908	1
AHD	Wax, yellow	18299202	1
Caelo	Wax, yellow	15023004	9
Alliance	Wax, yellow	280A130115	1
Alliance Health 14.04.2...	Wax, yellow	280A130115	1
Alliance Healthcare	Wax, yellow	290A120627	1
Bombastus	Wax, yellow	290A170915	1
Anzag	Wax, yellow	1462	1
Bombastus	Wax, yellow	279999	1
Bombastus	Wax, yellow	285109	1
Bombastus	Wax, yellow	296261	1
Bombastus	Wax, yellow	292025	1
Bombastus	Wax, yellow	caelo	1
Bombastus	Wax, yellow	267702	1
Bombastus	Wax, yellow	270682	3
Bombastus	Wax, yellow	17207405	1
Bombastus	Wax, yellow	17011604	1
cae	Wax, yellow	15317608	1
Caelo	Wax, yellow	12257022	3
Caelo	Wax, yellow	12367910	11
Caelo	Wax, yellow	6111407	1
Caelo	Wax, yellow	11017315	1
Caelo	Wax, yellow	11285001	2
Caelo	Wax, yellow	11308305	1
Caelo	Wax, yellow	11308311	2
Caelo	Wax, yellow	121248024-2015	1
Caelo	Wax, yellow	12124802	2
Caelo	Wax, yellow	11285014	2
Caelo	Wax, yellow	17121202	1
Caelo	Wax, yellow	17121201	1
Caelo	Wax, yellow	18121201	1
Caelo	Wax, yellow	12257009	7
Caelo	Wax, yellow	12124805	4
Caelo	Wax, yellow	12257002	3
Caelo	Wax, yellow	12041303	1
Caelo	Wax, yellow	12124814	2
Caelo	Wax, yellow	15041301	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Wax, yellow	13031201	4
Caelo	Wax, yellow	12367901	12
Caelo	Wax, yellow	22071301	1
Caelo	Wax, yellow	12367904	5
Caelo	Wax, yellow	13031206	8
Caelo	Wax, yellow	12124806	2
Caelo	Wax, yellow	10364810	1
Caelo	Wax, yellow	26091302	1
Caelo	Wax, yellow	30101308	1
Caelo	Wax, yellow	10121302	1
Caelo	Wax, yellow	11017308	1
Caelo	Wax, yellow	13335502	8
Caelo	Wax, yellow	17011403	1
Caelo	Wax, yellow	30011407	1
Caelo	Wax, yellow	4031403	1
Caelo	Wax, yellow	13335508	1
Caelo	Wax, yellow	17041402	1
Caelo	Wax, yellow	13051401	1
Caelo	Wax, yellow	13378603	1
Caelo	Wax, yellow	1335503	1
Caelo	Wax, yellow	13378630	2
Caelo	Wax, yellow	13335513	3
Caelo	Wax, yellow	12091404	1
Caelo	Wax, yellow	13335517	4
Caelo	Wax, yellow	13378602	1
Caelo	Wax, yellow	14189905	2
Caelo	Wax, yellow	13031221	1
Caelo	Wax, yellow	14189909	5
Caelo	Wax, yellow	13378639	3
Caelo	Wax, yellow	14189912	6
Caelo	Wax, yellow	28011501	1
Caelo	Wax, yellow	20031516	1
Caelo	Wax, yellow	20031517	1
Caelo	Wax, yellow	14336609	2
Caelo	Wax, yellow	13061503	1
Caelo	Wax, yellow	14336618	1
Caelo	Wax, yellow	20071503	1
Caelo	Wax, yellow	1436607	1
Caelo	Wax, yellow	15022902	7
Caelo	Wax, yellow	14336616	10
Caelo	Wax, yellow	15023003	4
Caelo	Wax, yellow	15292007	1
Caelo	Wax, yellow	15022907	1
Caelo	Wax, yellow	15317603	3
Caelo	Wax, yellow	1595	1
Caelo	Wax, yellow	15292014	20
Caelo	Wax, yellow	15292009	3
Caelo	Wax, yellow	14189920	1
Caelo	Wax, yellow	150622CF	1
Caelo	Wax, yellow	15317611	1
Caelo	Wax, yellow	161202CF/15317611	1
Caelo	Wax, yellow	16038203	10
Caelo	Wax, yellow	16038202	16
Caelo	Wax, yellow	16038206	19
Caelo	Wax, yellow	16034206	1
Caelo	Wax, yellow	16038207	9
Caelo	Wax, yellow	16038205	2
Caelo	Wax, yellow	290A0151214	1
Caelo	Wax, yellow	19041704	1
Caelo	Wax, yellow	16051702	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Wax, yellow	16038210	5
Caelo	Wax, yellow	17011605	1
Caelo	Wax, yellow	7091704	1
Caelo	Wax, yellow	5121707	1
Caelo	Wax, yellow	16163114	19
Caelo	Wax, yellow	1701611	1
Caelo	Wax, yellow	17011610	2
Caelo	Wax, yellow	17207404	2
Caelo	Wax, yellow	19031810	1
Caelo	Wax, yellow	18048906	20
Caelo	Wax, yellow	191372001	5
Caelo	Wax, yellow	10364837	1
Caelo	Wax, yellow	12367020	1
Caelo	Wax, yellow	14336605	2
Caelo	Wax, yellow	1214816	1
Caelo	Wax, yellow	15317601	6
Caelo	Wax, yellow	11017318	3
Caelo	Wax, yellow	12367915	8
Caelo	Wax, yellow	18299201	5
Caelo	Wax, yellow	12124801	4
Caelo	Wax, yellow	15317607	6
Caelo	Wax, yellow	13378634	6
Caelo	Wax, yellow	13378640	3
Caelo	Wax, yellow	14336608	3
Caelo	Wax, yellow	15317609	10
Caelo	Wax, yellow	12367921	1
Caelo	Wax, yellow	18113502	2
Caelo	Wax, yellow	1436616	1
Caelo	Wax, yellow	14189915	2
Caelo	Wax, yellow	1418915	1
Caelo	Wax, yellow	290A170915	4
Caelo	Wax, yellow	3253	1
Caelo	Wax, yellow	15317608	8
Caelo	Wax, yellow	18113507	1
Caelo	Wax, yellow	17011604	9
Caelo	Wax, yellow	17207402	18
Caelo	Wax, yellow	18049001	17
Caelo	Wax, yellow	18299208	2
Caelo	Wax, yellow	12367912	3
Caelo	Wax, yellow	14189907	2
Caelo	Wax, yellow	15098901	1
Caelo	Wax, yellow	17011611	7
Caelo	Wax, yellow	13335505	1
Caelo	Wax, yellow	13031220	3
Caelo	Wax, yellow	12124812	8
Caelo	Wax, yellow	12124810	4
Caelo	Wax, yellow	13335518	2
Caelo	Wax, yellow	13378636	1
Caelo	Wax, yellow	13335516	1
Caelo	Wax, yellow	15022904	4
Caelo	Wax, yellow	15292005	6
Caelo	Wax, yellow	17011607	13
Caelo	Wax, yellow	17207405	1
Caelo	Wax, yellow	14336607	11
Caelo	Wax, yellow	14189917	3
Caelo	Wax, yellow	14189914	4
Caelo	Wax, yellow	18049003	4
Caelo	Wax, yellow	12124816	1
Caelo	Wax, yellow	12367911	2
Caelo	Wax, yellow	4910A-01239	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Wax, yellow	13335509	2
Caelo	Wax, yellow	14189913	2
Caelo	Wax, yellow	15098902	1
Caelo	Wax, yellow	15023006	3
Caelo	Wax, yellow	152920004	1
Caelo	Wax, yellow	16163112	1
Caelo	Wax, yellow	17011612	22
Caelo	Wax, yellow	17207403	7
Caelo	Wax, yellow	18049002	2
Caelo	Wax, yellow	18113505	23
Caelo	Wax, yellow	12257012	3
Caelo	Wax, yellow	13031239	11
Caelo	Wax, yellow	12124817	2
Caelo	Wax, yellow	17011609	9
Caelo	Wax, yellow	1436620	1
Caelo	Wax, yellow	11017314	1
Caelo	Wax, yellow	133335507	1
Caelo	Wax, yellow	14G07-B04-300495	1
Caelo	Wax, yellow	12K20B05287421	1
Caelo	Wax, yellow	15292003	9
Caelo	Wax, yellow	1701607	1
Caelo	Wax, yellow	18113509	3
Caelo	Wax, yellow	19137202	5
Caelo	Wax, yellow	12367916-3429311150	1
Caelo	Wax, yellow	13031222	3
Caelo	Wax, yellow	14189901	1
Caelo	Wax, yellow	14189902	2
Caelo	Wax, yellow	14189919	2
Caelo	Wax, yellow	5022904	1
Caelo	Wax, yellow	14336617	1
Caelo	Wax, yellow	15022908	9
Caelo	Wax, yellow	15292004	13
Caelo	Wax, yellow	16038201	20
Caelo	Wax, yellow	15317613	8
Caelo	Wax, yellow	17011602	11
Caelo	Wax, yellow	170011602	1
Caelo	Wax, yellow	17011619	1
Caelo	Wax, yellow	170011607	2
Caelo	Wax, yellow	18113506	1
Caelo	Wax, yellow	15317610	6
Caelo	Wax, yellow	13031231	6
Caelo	Wax, yellow	12257004	2
Caelo	Wax, yellow	12124811	1
Caesar & Loretz	Wax, yellow	16038201	1
Caesar & Loretz	Wax, yellow	15317613	1
Caesar & Loretz GmbH	Wax, yellow	12367910	1
Caesar & Loretz GmbH	Wax, yellow	13031221	1
Caesar & Loretz GmbH	Wax, yellow	18299201	1
Caesar & Loretz GmbH	Wax, yellow	18299202	1
Caesar & Loretz GmbH	Wax, yellow	18299203	1
Caesar & Loretz GmbH / ...	Wax, yellow	15023004	1
Caesar & Loretz GmbH / ...	Wax, yellow	15317613	1
Caesar & Loretz GmbH / ...	Wax, yellow	18049001	1
Caesar & Loretz GmbH / ...	Wax, yellow	18113505	1
Caesar & Loretz GmbH, 4...	Wax, yellow	11285008	1
Caesar & Loretz GmbH, 4...	Wax, yellow	12367901	1
Caesar & Loretz GmbH, 4...	Wax, yellow	12367910	1
Caesar & Loretz GmbH, A...	Wax, yellow	18113505	1
Caesar & Loretz GmbH, Ph...	Wax, yellow	18049001	1
Caesar & Loretz GmbH/K	Wax, yellow	18113505	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH/Ph...	Wax, yellow	191372001	1
Caesar & Loretz/AHD	Wax, yellow	16038206	1
Caesar & Loretz/Gehe	Wax, yellow	19137202	1
Caesar & Loretz/Gehe	Wax, yellow	191372001	1
Caesar&Loretz GmbH	Wax, yellow	16038210	1
Caesar/Noweda	Wax, yellow	12124811	3
Caesar/Noweda	Wax, yellow	13031220	1
Caleo/Sanacorp	Wax, yellow	18299201	1
calo	Wax, yellow	17011612	1
Cealo/Gehe	Wax, yellow	13335502	1
E Plus	Wax, yellow	17011612	3
E-Plus	Wax, yellow	16038202	1
Euro OTC	Wax, yellow	1407013-01	1
Euro OTC	Wax, yellow	1503013-01	1
Euro OTC	Wax, yellow	1201012-01	1
Euro OTC	Wax, yellow	18113505	3
Euro/Sanacorp	Wax, yellow	1708506	1
Euroo	Wax, yellow	1407013-01	1
Euro OTC	Wax, yellow	17011607	1
Fagron	Wax, yellow	13B04-N04	2
Fagron	Wax, yellow	13L02-B01-294113	2
Fagron	Wax, yellow	13L02-B01-291452	1
Fagron	Wax, yellow	13L02-B01-294114	1
Fagron	Wax, yellow	280A140306	1
Fagron	Wax, yellow	15317603	1
Fagron	Wax, yellow	17011607	1
Fagron	Wax, yellow	12D23-N05	2
Fagron	Wax, yellow	14G07-B04-300495	2
Fagron	Wax, yellow	13102-B01	1
Finze	Wax, yellow	10145002	1
Gehe	Wax, yellow	12079412	1
Gehe	Wax, yellow	12367910	1
Gehe	Wax, yellow	16038207	1
Gehe	Wax, yellow	19137202	1
GEHE	Wax, yellow	13335502	1
GEHE	Wax, yellow	18113501	1
Caelo	Wax, yellow	18113503	1
Geibo	Wax, yellow	290A170915	1
Klenk	Wax, yellow	160311	1
Klenk	Wax, yellow	190A170314	1
Hirsch	Wax, yellow	12257012	1
Ichthyol	Wax, yellow	13031239	1
Kehr	Wax, yellow	18113501	1
Klenk	Wax, yellow	280A110110	1
Klenk	Wax, yellow	280A120627	5
Klenk	Wax, yellow	290A120627	4
Klenk	Wax, yellow	280-A120627	1
Klenk	Wax, yellow	280A130115	26
Klenk	Wax, yellow	290A081210	1
Klenk	Wax, yellow	280A13011A	1
Klenk	Wax, yellow	13335513	1
Klenk	Wax, yellow	290A140903	5
Klenk	Wax, yellow	282A140306	1
Klenk	Wax, yellow	290A150716	4
Klenk	Wax, yellow	416E01240	1
Klenk	Wax, yellow	290A170915	5
Klenk	Wax, yellow	282A120627	1
Klenk	Wax, yellow	290A170314	3
Klenk	Wax, yellow	290A110803	1
Klenk	Wax, yellow	280A140306	7

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Wax, yellow	280A150528	12
Klenk	Wax, yellow	280A171019	15
L10	Wax, yellow	17207403	1
L12	Wax, yellow	18113502	1
L12	Wax, yellow	18113506	1
Mittelwand bio 2017	Wax, yellow	5022017	1
Noweda	Wax, yellow	280A120627	2
Noweda	Wax, yellow	12124810	1
Noweda	Wax, yellow	150230004	1
Noweda	Wax, yellow	15023002	1
Klenk	Wax, yellow	290A151214	5
Caelo	Wax, yellow	12330116	1
Caelo	Wax, yellow	14189908	1
Euro OTC	Wax, yellow	16038201	1
Pharmachem	Wax, yellow	16038202	1
PHOENIX 24.07.2014	Wax, yellow	13001206	1
Phoenix goettingen 08.05	Wax, yellow	15098901	1
phönix	Wax, yellow	16038207	1
Phönix	Wax, yellow	12367901	1
Phönix	Wax, yellow	12367904	1
Phönix	Wax, yellow	13031206	1
Phönix	Wax, yellow	12367915	1
Phönix	Wax, yellow	15317609	1
Phönix	Wax, yellow	16038206	1
PHÖNIX	Wax, yellow	17011611	1
Caelo	Wax, yellow	18113501	28
Sanacorp	Wax, yellow	12257009	1
Sanacorp	Wax, yellow	12367910	1
Sanacorp	Wax, yellow	13335502	1
Sanacorp	Wax, yellow	13378619	1
Sanacorp	Wax, yellow	16038203	1
Sanacorp	Wax, yellow	17011604	2
Sanacorp	Wax, yellow	17011609	1
Sanacorp	Wax, yellow	17011612	1
Sanacorp	Wax, yellow	18113502	1
Sanacorp	Wax, yellow	18113501	1
Sanacorp WE:18.04.16 EK...	Wax, yellow	15023004	1
Caelo	Wax, yellow	11285015	1
Caelo	Wax, yellow	12124807	3
Fagron	Wax, yellow	14336616	1
Caelo	Wax, yellow	12367916	6
Caelo	Wax, yellow	13335503	6
Caelo	Cetyl palmitate 15	15301703	9
Caelo	Cetyl palmitate 15	14351606	4
Caelo	Cetyl palmitate 15	12331916	8
Caelo	Cetyl palmitate 15		5
Caelo	Cetyl palmitate 15	17043503	6
Caelo	Cocoa butter	13292013	9
Caelo	Cocoa butter	14348906	8
Caelo	Cocoa butter	17055907	15
Bombastus	Hard fat in pastilles	306363	4
Caelo	Hard fat in pastilles	12158122	1
Fagron	Hard fat in pastilles		1
Fagron	Hard fat W35	15A07-B12-309245	1
Caelo	Paraffin, hard	13390413	1
Caelo	Paraffin, hard	15232004	7
Caelo	Sodium dodecyl sulfate	13099011	3
Caelo	Sodium dodecyl sulfate	15344503	4
Caelo	Sodium dodecyl sulfate	16229217	5
Caelo	Wax, bleached	14336620	7

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Wax, bleached	15292022	9
Caelo	Wax, yellow	13335507	6
Caelo	Wax, yellow	13378619	13
Caelo	Wax, yellow	15317602	4
Sanacorp	Wax, yellow		1
Wachs neu	Wax, yellow		2

- 108 541 spectra from 742 *Apo-Ident* customers from a total of 31 188 batches from a further 698 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Waxes / Fats* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Waxes / Fats* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	1907	0	108 782
Type B	0	1043	10	118 089
Type C	0	2634	72	108 541

The substance/substance group *Waxes / Fats* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9903 %)	100.0000 % (> 99.6854 %)
Type B	100.0000 % (> 99.9893 %)	99.0503 % (> 98.7654 %)
Type C	100.0000 % (> 99.8899 %)	97.3392 % (> 97.2284 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra ([Rule of Three](#) [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Waxes / Fats* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium stearate	17.80	—
Poloxamers 407	40.54	—
Stearic acid 50	43.18	—
Wool alcohols	54.55	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Waxes / Fats* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21682	21682	0.00	21.78
21766	22330	1.91	22.73
22330	22330	0.00	23.05
21483	21483	0.00	19.74
24720	24720	0.00	27.09
21067	22479	5.37	44.68
22479	22479	0.00	44.54
23565	22479	18.59	46.28
23705	22479	18.59	47.31
21880	21880	0.00	43.52
22338	21880	2.54	44.13
23601	21880	2.57	41.03
25047	21880	5.13	39.02
21433	23511	2.27	24.44
22245	23511	4.04	23.44
23511	23511	0.00	24.22
24870	23511	2.68	24.51
24716	24716	0.00	36.22
21731	22349	1.81	25.05
22349	22349	0.00	25.48
22352	20986	6.95	38.04
23242	24715	6.54	39.01
23278	23278	0.00	36.02
20865	20865	0.00	28.84
21875	23639	3.62	25.67
21984	21984	0.00	27.04
22325	21984	2.90	26.42
22486	22486	0.00	25.50
21482	24813	5.89	48.64
23560	23817	3.62	26.57
22348	23067	4.56	46.59
23639	23639	0.00	25.19
23067	23067	0.00	48.73
23817	23817	0.00	24.91

continued on the next page

continued from previous page

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
23707	23067	3.88	55.07
24813	24813	0.00	48.74
24715	24715	0.00	35.55
22244	23511	5.41	25.42
22956	23511	11.60	24.66
20986	20986	0.00	40.45

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Wool alcohols**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20495-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Wool alcohols; Alcoholes lanae

Special notes

When selecting the *Wool alcohols* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wool alcohols	4	2	15

Second-stage model

For differentiation of the substance/substance group *Wool alcohols* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Wool alcohols*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Wool alcohols	13380601	21520	40	1412037
Caelo	Wool alcohols	153703	22328	60	20151111*
Caelo	Wool alcohols	153703	22329	60	20151111*
Caelo	Wool alcohols	163530	23098	40	20161223*
Caelo	Wool alcohols	191275	24722	40	20190606*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 240 spectra of 5 reference samples from the substance/substance group *Wool alcohols*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 449 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 80 spectra of 2 reference samples from the substance/substance group *Wool alcohols*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Wool alcohols	173160	23972	40
Caelo	Wool alcohols	181619	24165	40

- 119 062 spectra from a total of 2418 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 24 spectra from 14 *Apo-Ident* customers from 16 batches from the substance/substance group *Wool alcohols*.
- Among them are spectra of independent samples from 15 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Wool alcohols	12340505	1
Caelo	Wool alcohols	13083912	1
Caelo	Wool alcohols	11011401	1
Caelo	Wool alcohols	23101408	1
Caelo	Wool alcohols	13226408	1
Caelo	Wool alcohols	13071502	1
Caelo	Wool alcohols	15304502	1
Caelo	Wool alcohols	6111801	1
Caelo	Wool alcohols	4/2015	1
Caelo	Wool alcohols	14262501	1
Caelo	Wool alcohols	15304505	3
Caelo	Wool alcohols	17169701	3
Caelo/ Noweda	Wool alcohols	13380601	1
Fagron	Wool alcohols	16235702	1
Caelo	Wool alcohols	13083906	2
Caelo	Wool alcohols	18092502	3
Caelo	Wool alcohols	13380601	1

- 111 223 spectra from 742 *Apo-Ident* customers from a total of 31 875 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Wool alcohols* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wool alcohols* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	240	0	110 449
Type B	0	80	0	119 062
Type C	0	24	0	111 223

The substance/substance group *Wool alcohols* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 75.0000 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wool alcohols* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Magnesium stearate	39.53	—
Soy lecithin (instant form)	44.22	—
Deoxycholic acid	48.68	—
Ascorbyl palmitate	51.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wool alcohols* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21520	21520	0.00	50.59
22328	22328	0.00	57.35
22329	22329	0.00	57.35
23098	23098	0.00	53.33
24722	24722	0.00	55.82

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Xylitol**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20994-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xylitol; Xylitolum

Special notes

When selecting the *Xylitol* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xylitol	4	3	17

Second-stage model

For differentiation of the substance/substance group *Xylitol* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xylitol*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Xylitol	14068206	21755	60	20140317
Caelo	Xylitol	15135405	22248	60	20150417
Caelo	Xylitol	15135405	22579	40	20150417
Fagron	Xylitol	14G04-B04-298356	21754	60	AR-15-FG-008046-01
Fagron	Xylitol	14G04-B04-303524	22254	60	20140919

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 5 reference samples from the substance/substance group *Xylitol*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 409 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Xylitol*.
- Among them are spectra of independent samples from 3 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Xylitol	15388101	22578	40
Caelo	Xylitol	163174	23061	40
Caelo	Xylitol	181133	24041	40

- 119 022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 28 spectra from 14 *Apo-Ident* customers from 20 batches from the substance/substance group *Xylitol*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Xylitol	13230305	1
Caelo	Xylitol	13230309	1
Caelo	Xylitol	14061401	1
Caelo	Xylitol	16317401	1
Caelo	Xylitol	15388104	2
Caelo	Xylitol	5112I-02787	1
Caelo	Xylitol	13230315	1
Caelo	Xylitol	3314M-02787	1
Caelo	Xylitol	18045302	4
Caelo	Xylitol	13230302	1
Caelo	Xylitol	12240612	1
Caelo	Xylitol	14G04-B04-298356	2
Fagron	Xylitol	13/23-N06	1
Fagron	Xylitol	16c14-B02-320887	1
Fagron	Xylitol	13H28N10	1
Fagron	Xylitol	12J25-N06	2
Fagron	Xylitol	13H28-N10	2
Caelo	Xylitol	18113304	1
Caelo	Xylitol	14068206	1
Fagron	Xylitol	14G04-B04-303524	2

- 111 219 spectra from 742 *Apo-Ident* customers from a total of 31 871 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xylitol* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xylitol* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	120	0	119 022
Type C	0	28	0	111 219

The substance/substance group *Xylitol* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 78.5714 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xylitol* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neomycin sulfate	24.69	—
Galactose	40.18	—
Sodium citrate	44.24	—
Potassium citrate	45.57	—
Aciclovir	47.42	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xylitol* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21754	21754	0.00	32.05
21755	21754	6.84	23.38
22248	21754	6.47	23.60
22254	21754	3.45	30.94
22579	21754	6.57	24.30

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Xylometazoline hydrochloride**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20025-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xylometazoline hydrochloride; Xylometazolini hydrochloridum

Special notes

When selecting the *Xylometazoline hydrochloride* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xylometazoline hydrochloride	4	2	54

Second-stage model

For differentiation of the substance/substance group *Xylometazoline hydrochloride* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xylometazoline hydrochloride*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Xylometazoline h...	13344901	21516	60	1501655
Caelo	Xylometazoline h...	13344901	21517	60	20131119
Caelo	Xylometazoline h...	16074211	23246	40	20160318
Fagron	Xylometazoline h...	13I18-B03-295481	21722	60	AR-15-FG-007785-01
Fagron	Xylometazoline h...	14K19-B05-305006	21927	60	20141128
Fagron	Xylometazoline h...	14K19-B05-305006	21927SI	60	20141128

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 340 spectra of 6 reference samples from the substance/substance group *Xylometazoline hydrochloride*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 349 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 340 spectra of 8 reference samples from the substance/substance group *Xylometazoline hydrochloride*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Xylometazoline hydrochloride	170739	23314	40
Caelo	Xylometazoline hydrochloride	173457	23832	40
Caelo	Xylometazoline hydrochloride	13344901	21517SI [†]	60
Caelo	Xylometazoline hydrochloride	16074211	23246SI [†]	40
Caelo	Xylometazoline hydrochloride	170739	23314SI	40
Caelo	Xylometazoline hydrochloride	170739	23320	40
Caelo	Xylometazoline hydrochloride	170739	23320SI	40
Caelo	Xylometazoline hydrochloride	173457	23832SI	40

- 118 802 spectra from a total of 2416 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 134 spectra from 93 *Apo-Ident* customers from 55 batches from the substance/substance group *Xylometazoline hydrochloride*.
- Among them are spectra of independent samples from 54 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Anzag	Xylometazoline hydrochloride	12027911	1
Anzag	Xylometazoline hydrochloride	15037907	2
Caelo	Xylometazoline hydrochloride	24111202	1
Caelo	Xylometazoline hydrochloride	9276404	1
Caelo	Xylometazoline hydrochloride	12287210	7
Caelo	Xylometazoline hydrochloride	9278404	1
Caelo	Xylometazoline hydrochloride	12287212	2
Caelo	Xylometazoline hydrochloride	2031502	1
Caelo	Xylometazoline hydrochloride	13344908	1
Caelo	Xylometazoline hydrochloride	15037907	4
Caelo	Xylometazoline hydrochloride	15037906	1
Caelo	Xylometazoline hydrochloride	15037910	2
Caelo	Xylometazoline hydrochloride	15037912	1
Caelo	Xylometazoline hydrochloride	15292812	2
Caelo	Xylometazoline hydrochloride	16074205	5
Caelo	Xylometazoline hydrochloride	16074209	6
Caelo	Xylometazoline hydrochloride	16074216	3
Caelo	Xylometazoline hydrochloride	160740209	1
Caelo	Xylometazoline hydrochloride	16074217	3
Caelo	Xylometazoline hydrochloride	160742095416	1
Caelo	Xylometazoline hydrochloride	23051820	1
Caelo	Xylometazoline hydrochloride	17345706	1
Caelo	Xylometazoline hydrochloride	17073905	7
Caelo	Xylometazoline hydrochloride	13171205	1
Caelo	Xylometazoline hydrochloride	15292803	3
Caelo	Xylometazoline hydrochloride	10118821	2

continued on the next page

[†]These spectra were recorded from material of the same package as the corresponding calibration spectra (*Type A*). Hence, these spectra are not independent and are not of *Type B*.

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Xylometazoline hydrochloride	12287203	8
Caelo	Xylometazoline hydrochloride	17345703	5
Caelo	Xylometazoline hydrochloride	12287201	2
Caelo	Xylometazoline hydrochloride	16074202	1
Caelo	Xylometazoline hydrochloride	17345707	3
Caelo	Xylometazoline hydrochloride	17345708	2
Caelo	Xylometazoline hydrochloride	12027906	2
Caelo	Xylometazoline hydrochloride	17073908	1
Caelo	Xylometazoline hydrochloride	15292811	1
Caelo	Xylometazoline hydrochloride	12287213	1
Caelo	Xylometazoline hydrochloride	181102181	1
Caelo	Xylometazoline hydrochloride	12287204	2
Caelo	Xylometazoline hydrochloride	1703902	1
Caelo	Xylometazoline hydrochloride	16074201	3
Caelo	Xylometazoline hydrochloride	13171202	10
Caelo	Xylometazoline hydrochloride	13171203	2
Caelo	Xylometazoline hydrochloride	17073902	2
Caesar & Loretz GmbH	Xylometazoline hydrochloride	17073902	1
Celoa vdL	Xylometazoline hydrochloride	13171202	1
Fagron	Xylometazoline hydrochloride	13E06-N11	1
Fagron	Xylometazoline hydrochloride	13171203	1
Fagron	Xylometazoline hydrochloride	10416XMHC	1
Fagron	Xylometazoline hydrochloride	12287210	1
Fagron	Xylometazoline hydrochloride	15Jo6-B99-313751	1
Fagron	Xylometazoline hydrochloride	1318-B03-295479	1
Fagron	Xylometazoline hydrochloride	12G31-N01	1
Gehe	Xylometazoline hydrochloride	10118802	1
GEHE	Xylometazoline hydrochloride	16074209	1
Nachprüfung	Xylometazoline hydrochloride	4317E-03337	1
Noweda	Xylometazoline hydrochloride	12027902	1
Noweda	Xylometazoline hydrochloride	12287203	1
Fagron	Xylometazoline hydrochloride	13I09-N02	1
Caelo	Xylometazoline hydrochloride	15292804	4
Caelo	Xylometazoline hydrochloride	17073909	2
Sanacorp	Xylometazoline hydrochloride	12027902	1
Sanacorp	Xylometazoline hydrochloride	15037906	1
Sanacorp	Xylometazoline hydrochloride	17345703	1
Caelo	Xylometazoline hydrochloride	153037907	1
Caelo	Xylometazoline hydrochloride	13344901	1

- 111 113 spectra from 742 *Apo-Ident* customers from a total of 31 836 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xylometazoline hydrochloride* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xylometazoline hydrochloride* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	340	0	110 349
Type B	0	340	0	118 802
Type C	0	129	5	111 113

The substance/substance group *Xylometazoline hydrochloride* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 98.2353 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.2353 %)
Type C	100.0000 % (> 99.8899 %)	96.2687 % (> 94.0299 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xylometazoline hydrochloride* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ornithine aspartate	25.24	—
Methacholine chloride	42.14	—
Tetracaine base	42.70	—
Tretinoin	49.70	—
Ibuprofen	52.47	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xylometazoline hydrochloride* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21516	21516	0.00	41.60
21517	21516	2.95	42.28
21722	21722	0.00	42.59
21927	21722	5.57	43.55
23246	21722	3.66	42.78

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Xylose**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20517-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Xylose; Xylosum

Special notes

When selecting the *Xylose* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Xylose	4	5	20

Second-stage model

For differentiation of the substance/substance group *Xylose* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Xylose*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Xylose	14218902	21606	60	AR-14-FG-013086-01
Caelo	Xylose	17160902	23413	40	20170704
Fagron	Xylose	13A31-B40-292395	21763	60	20140407
Fagron	Xylose	16A25-B05-328261	23524	40	20160215

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 200 spectra of 4 reference samples from the substance/substance group *Xylose*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 110 489 spectra from a total of 1962 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 200 spectra of 5 reference samples from the substance/substance group *Xylose*.
- Among them are spectra of independent samples from 5 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Xylose	13133402	20868	40
Caelo	Xylose	162064	22758	40
Caelo	Xylose	171609	23656	40
Caelo	Xylose	173188	23849	40
Caelo	Xylose	190499	24527	40

- 118942 spectra from a total of 2415 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 28 spectra from 10 *Apo-Ident* customers from 22 batches from the substance/substance group *Xylose*.
- Among them are spectra of independent samples from 20 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Xylose	13133404	2
Caelo	Xylose	13133410	1
Caelo	Xylose	12120101	1
Caelo	Xylose	5031501	1
Caelo	Xylose	11031501	1
Caelo	Xylose	16002302	2
Caelo	Xylose	16002309	1
Caelo	Xylose	16206405	1
Caelo	Xylose	16002301	1
Caelo	Xylose	17160905	1
Caelo	Xylose	13133414	3
Ebert & Jacobi 12.07...	Xylose	16002301	2
Eigenherstellung	Xylose	80414HJK01	1
Fagron	Xylose	28111405	1
Fagron	Xylose	10121401	1
Fagron	Xylose	14E-B03_300658	1
Fagron	Xylose	13133415	1
Fagron	Xylose	80414PJK01	1
Falcento	Xylose	2013051801	1
Phoenix 20.06.2014	Xylose	13A31-B04-292396	1
Phoenix Goettin	Xylose	13133422	1
Caelo	Xylose	17160902	1
Euro OTC	Xylose		1

- 111219 spectra from 742 *Apo-Ident* customers from a total of 31869 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Xylose* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Xylose* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	200	0	110 489
Type B	0	200	0	118 942
Type C	0	28	0	111 219

The substance/substance group *Xylose* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 78.5714 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Xylose* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Isosorbide dinitrate 40%	56.85	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Xylose* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
21606	21606	0.00	53.47
21763	21606	12.63	58.93
23413	21606	11.52	59.61
23524	21606	12.24	59.81

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Zinc acetate dihydrate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20398-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zinc acetate dihydrate; Zincum aceticum purum

Special notes

When selecting the *Zinc acetate dihydrate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zinc acetate dihydrate	3	2	17

Second-stage model

For differentiation of the substance/substance group *Zinc acetate dihydrate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zinc acetate dihydrate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Zinc acetate dihyd...	15383301	22728	40	20151127
Caelo	Zinc acetate dihyd...	153833	23030	40	20151127*
Caelo	Zinc acetate dihyd...	170204	23031	40	20170126*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 120 spectra of 3 reference samples from the substance/substance group *Zinc acetate dihydrate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 110 569 spectra from a total of 1963 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 120 spectra of 3 reference samples from the substance/substance group *Zinc acetate dihydrate*.
- Among them are spectra of independent samples from 2 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Zinc acetate dihydrate	17020404	23514	40
Caelo	Zinc acetate dihydrate	182046	24213	40
Caelo	Zinc acetate dihydrate	170204	23637	40

- 119022 spectra from a total of 2417 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 34 spectra from 32 *Apo-Ident* customers from 18 batches from the substance/substance group *Zinc acetate dihydrate*.
- Among them are spectra of independent samples from 17 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Zinc acetate dihydrate	12134803	1
Caelo	Zinc acetate dihydrate	12134801	2
Caelo	Zinc acetate dihydrate	12316403	2
Caelo	Zinc acetate dihydrate	12316404	2
Caelo	Zinc acetate dihydrate	14133201	1
Caelo	Zinc acetate dihydrate	15160804	1
Caelo	Zinc acetate dihydrate	15160801	1
Caelo	Zinc acetate dihydrate	15383306	3
Caelo	Zinc acetate dihydrate	17020404	2
Caelo	Zinc acetate dihydrate	17197601	7
Caelo	Zinc acetate dihydrate	15383304	1
Caelo	Zinc acetate dihydrate	12316405	1
Caelo	Zinc acetate dihydrate	17365807	1
Caelo	Zinc acetate dihydrate	17020403	2
Caelo	Zinc acetate dihydrate	12316401	2
Caelo	Zinc acetate dihydrate	18204604	2
Caelo	Zinc acetate dihydrate	15383308	2
phönix	Zinc acetate dihydrate	15383301	1

- 111213 spectra from 742 *Apo-Ident* customers from a total of 31873 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zinc acetate dihydrate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Zinc acetate dihydrate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	120	0	110 569
Type B	0	119	1	119 022
Type C	0	18	16	111 213

The substance/substance group *Zinc acetate dihydrate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9893 %)	99.1667 % (> 96.6667 %)
Type C	100.0000 % (> 99.8899 %)	52.9412 % (> 44.1176 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zinc acetate dihydrate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Choline hydrogen tartrate	43.94	—
Ornithine aspartate	44.53	—
Serine	63.99	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zinc acetate dihydrate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22728	23030	2.94	45.86
23030	23030	0.00	47.48
23031	23031	0.00	44.53

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

VALIDATION REPORT

IdentModule 2.2-2020-04

Validated substance/substance group **Zinc gluconate**
Substance class APIs & excipients, solid
Report date 14/07/2020
Report number 20379-2020-07-14
Executing company HiperScan GmbH
Weißeritzstraße 3
01067 Dresden
Germany

Relevant substance names

Zinc gluconate; Zincum gluconicum

Special notes

When selecting the *Zinc gluconate* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-6679-5 *European Pharmacopoeia 9th Edition, Basic Version 2017* [3]
Komm2.2.40 *Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident* [4]
AA004 *Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also “database”) in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Zinc gluconate	6	8	16

Second-stage model

For differentiation of the substance/substance group *Zinc gluconate* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the [chemometric models](#). The following samples have been obtained from the substance/substance group *Zinc gluconate*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Zinc gluconate	170165	23034	40	20170125*
Caelo	Zinc gluconate	170951	23292	40	20170518*
Euro OTC	Zinc gluconate	1407033-02	21709	60	20140902
Euro OTC	Zinc gluconate	1508007	21882	60	20150827*
Euro OTC	Zinc gluconate	1603035	22513	40	20160427*
Euro OTC	Zinc gluconate	1807019	24150	40	20180725*

Validation samples

A total of 341 078 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 280 spectra of 6 reference samples from the substance/substance group *Zinc gluconate*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 110 409 spectra from a total of 1960 batches from further 390 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a [†]. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 320 spectra of 8 reference samples from the substance/substance group *Zinc gluconate*.

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Zinc gluconate	161788	22619	40
Euro OTC	Zinc gluconate	1606018	22700	40
Euro OTC	Zinc gluconate	1701017	22994	40
Euro OTC	Zinc gluconate	1706009	23544	40
Euro OTC	Zinc gluconate	1711004	23730	40
Euro OTC	Zinc gluconate	1810014	24347	40
Euro OTC	Zinc gluconate	1902017	24635	40
Euro OTC	Zinc gluconate	1910010	24942	40

- 118 822 spectra from a total of 2412 batches from further 799 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix B](#).

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 225 spectra from 8 *Apo-Ident* customers from 17 batches from the substance/substance group *Zinc gluconate*.
- Among them are spectra of independent samples from 16 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Caelo	Zinc gluconate	16178801	1
Caelo	Zinc gluconate	17016502	2
Caelo	Zinc gluconate	17095103	1
Euro OTC	Zinc gluconate	1606018-01	4
Euro OTC	Zinc gluconate	1606018-02	36
Euro OTC	Zinc gluconate	1701017-01	31
Euro OTC	Zinc gluconate	1706009-01	66
Euro OTC	Zinc gluconate	1711004-01	27
Euro OTC	Zinc gluconate	1709012-0103707875	1
Euro OTC	Zinc gluconate	170901201	9
Euro OTC	Zinc gluconate	1312010-01	1
Euro OTC	Zinc gluconate	27061711	1
Euro OTC	Zinc gluconate	1807019-01	14
Fagron	Zinc gluconate	14J30-B06-300520	1
KOKO GmbH	Zinc gluconate	1810014-01	28
Euro OTC	Zinc gluconate	1405011-01	1
Euro OTC	Zinc gluconate	1807019	1

- 111 022 spectra from 742 *Apo-Ident* customers from a total of 31 875 batches from a further 706 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this [chemometric model](#), the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix C](#).

Validation results

The validation runs checked whether the substance/substance group *Zinc gluconate* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all

relevant spectra of the various substances were compared with *Zinc gluconate* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

	False positive	True positive	False negative	True negative
Type A	0	280	0	110 409
Type B	0	320	0	118 822
Type C	0	225	0	111 022

The substance/substance group *Zinc gluconate* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate (specificity)* and the weighted *true positive rate (recognition rate)* are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9904 %)	100.0000 % (> 97.8571 %)
Type B	100.0000 % (> 99.9893 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 99.8899 %)	100.0000 % (> 97.3333 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.

Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Zinc gluconate* in the substance class *APIs & excipients, solid*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Tobramycin sulfate	18.92	—
Aciclovir	35.04	—
Neomycin sulfate	36.43	—
Trometamol	44.38	—
Arginine	47.26	—
Magnesium citrate	47.76	—
Uridine	50.84	—

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Zinc gluconate* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
22513	22513	0.00	25.95
24150	24150	0.00	19.31
21709	23292	5.51	18.92
21882	21882	0.00	25.62
23034	23034	0.00	22.74
23292	23292	0.00	22.19

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.

Appendix A: Additional calibration samples (*Type A*)

Substance spectra also enter the generation of the [chemometric model](#) which cannot be identified with this model. This serves the purpose that substances which the model is not supposed to recognise are safely rejected. The spectra of these samples are entered into the validation as *Type A*. They were recorded by *HiperScan GmbH*.

The samples originate from 191 batches. From these, 9421 spectra were recorded. The calibration spectra of substances which can be identified with the model are listed respectively in the section *calibration samples* for the individual substances and do not appear again elsewhere in this list.

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Aluminium potassium sulfate dodecahydrate	12144605	40	from supplier
Caelo	Amphetamine sulfate	13344603	40	0814J-03361
Caelo	Amphetamine sulfate	16153902	40	2017A-03361
Caelo	Amphetamine sulfate	13344603	60	0814J-03361
Fagron	Amphetamine sulfate	13G08-N11	40	0814K-03361
Fagron	Amphetamine sulfate	15L01-B05-315291	60	1316Q-03361
Fagron	Amphetamine sulfate	13G08-N11	60	0814K-03361
Fagron	Amphetamine sulfate	15L01-B05-315291	60	1316Q-03361
Th. Geyer	Amphetamine sulfate	67002	40	0814I-03361
Th. Geyer	Amphetamine sulfate	067043	40	2017C-03361
Th. Geyer	Amphetamine sulfate	67002	60	0814I-03361
Flora Apothek...	Amygdalin	13121802	40	1405619
Auropure Life...	Amygdalin, bitter almond extract 98%	PA02099-17102131	40	from supplier
Safic-Alcan	Amygdalin, bitter almond extract 98%	BAE150902	60	from supplier
Safic-Alcan	Amygdalin, bitter almond extract 98%	BAE150902	60	from supplier
Fagron	Barbital sodium	12F27-N02	40	0814I-07775
Fagron	Barbital sodium	14K14-B04-303353	60	1516I-07775
Fagron	Barbital sodium	12F27-N02	60	0814I-07775
Fagron	Barbital sodium	14K14-B04-303353	60	1516I-07775
Sigma-Aldrich	Betamethasone acetate	LRAA8500	40	CRS
Sigma-Aldrich	Betamethasone sodium phosphate	MKBS9676V	40	CRS
Caelo	Bilberry fruit, dried	10265602	40	20101206
Caelo	Black mustard seed, powdered	12350204	80	1403711
Flora Apothek...	Calcium colamine phosphate	14384	40	from supplier
Th. Geyer	Calcium colamine phosphate	33299	60	from supplier
Th. Geyer	Calcium colamine phosphate	66606	40	from supplier
Caelo	Chicory root, cut	11374504	40	20120112
Euro OTC	Cholecalciferol dry concentrate	2001007	40	20200316*
Caelo	Cocaine hydrochloride	13259305	40	0814J-01278
Caelo	Cocaine hydrochloride	15224802	60	1316Q-01278
Caelo	Cocaine hydrochloride	15224802	60	1316Q-01278
Caelo	Cocaine hydrochloride	17003902	40	1917S-01278
Caelo	Cocaine hydrochloride	13259305	60	0814J-01278
Caelo	Cocaine hydrochloride	15224802	60	1316Q-01278
Caelo	Cocaine hydrochloride	15224802	60	1316Q-01278
Fagron	Cocaine hydrochloride	13I17-N02	40	0814I-01278
Fagron	Cocaine hydrochloride	16B11-B05-323386	40	1917Q-1278
Fagron	Cocaine hydrochloride	13I17-N02	60	0814I-01278
Th. Geyer	Cocaine hydrochloride	60145	40	0814K-01278

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Supplier	Substance	Batch	Spectra	Certificate
Th. Geyer	Cocaine hydrochloride	60145	60	0814K-01278
Caelo	Codeine phosphate hemihydrate	13071504	40	0814J-01279
Caelo	Codeine phosphate hemihydrate	15350703	60	1316R-01279
Caelo	Codeine phosphate hemihydrate	13071504	60	0814J-01279
Caelo	Codeine phosphate hemihydrate	15350703	60	1316R-01279
Fagron	Codeine phosphate hemihydrate	13C11-N10	40	0814I-01279
Fagron	Codeine phosphate hemihydrate	15F09-B02-310520	60	1316Q-01279
Fagron	Codeine phosphate hemihydrate	16E17-B05-324109	40	2017A-01279
Fagron	Codeine phosphate hemihydrate	13C11-N10	60	0814I-01279
Fagron	Codeine phosphate hemihydrate	15F09-B02-310520	60	1316Q-01279
Th. Geyer	Codeine phosphate hemihydrate	67038	40	0814K-01279
Th. Geyer	Codeine phosphate hemihydrate	067054	40	2017D-01279
Th. Geyer	Codeine phosphate hemihydrate	67038	60	0814K-01279
Euro OTC	Deoxycholic acid	1305051-01	40	from supplier
New Zealand P...	Deoxycholic acid	0416720	40	from supplier
Fagron	Dexamphetamine sulfate	13I23-N01	40	0814M-03582
Fagron	Dexamphetamine sulfate	15H06-B04-313862	60	1316Q-03582
Fagron	Dexamphetamine sulfate	16D20-B01-321049	40	2017B-03582
Fagron	Dexamphetamine sulfate	13I23-N01	60	0814M-03582
Fagron	Dexamphetamine sulfate	15H06-B04-313862	60	1316Q-03582
Sigma-Aldrich	Diclofenac potassium	D1039990	40	CRS
Caelo	Dihydrocodeine hydrogen tartrate	13267601	40	0914A-03065
Caelo	Dihydrocodeine hydrogen tartrate	12142506	40	0914B-03065
Caelo	Dihydrocodeine hydrogen tartrate	15295901	60	1316Q-03065
Caelo	Dihydrocodeine hydrogen tartrate	13267601	60	0914A-03065
Caelo	Dihydrocodeine hydrogen tartrate	12142506	60	0914B-03065
Caelo	Dihydrocodeine hydrogen tartrate	15295901	60	1316Q-03065
Fagron	Dihydrocodeine hydrogen tartrate	13H19-N03	40	0914C-03065
Fagron	Dihydrocodeine hydrogen tartrate	14K26-B04-306298	60	1516I-03065
Fagron	Dihydrocodeine hydrogen tartrate	15F18-B07-323388	40	2017A-03065
Fagron	Dihydrocodeine hydrogen tartrate	13H19-N03	60	0914C-03065
Th. Geyer	Dihydrocodeine hydrogen tartrate	67035	40	0914D-03065
Th. Geyer	Dihydrocodeine hydrogen tartrate	067052	40	2017D-03065
Th. Geyer	Dihydrocodeine hydrogen tartrate	67035	60	0914D-03065
Safic-Alcan	Dimercaptosuccinic acid	20170210	40	from supplier

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Supplier	Substance	Batch	Spectra	Certificate
Fagron	Fentanyl citrate	13G30-N06	40	0814M-07678
Fagron	Fentanyl citrate	15F18-B01-525098	60	1316R-03686
Fagron	Fentanyl citrate	15F18-B01-525166	60	1316Q-03686
Fagron	Fentanyl citrate	13G30-N06	60	0814M-07678
Fagron	Fentanyl citrate	15F18-B01-525098	60	1316R-03686
Fagron	Fentanyl citrate	15F18-B01-525166	60	1316Q-03686
EDQM	Fenticonazole nitrate	1.3	40	CRS
Caelo	Ginger, peeled	11325715	40	20111205
Flora Apothek. ...	Glycyrrhizic acid	10588	40	from supplier
Euro OTC	Griffonia seed extract	1205027	40	from supplier
Euro OTC	Griffonia seed extract	1705007	40	20170601*
Euro OTC	Griffonia seed extract	1905017	40	20190709*
Pharmorgana	Griffonia seed extract	1000200297	40	from supplier
Caelo	Hay flower	12317104	40	20121122
Klenk	Hay flower	1400A130304	40	20130403
Fagron	Hydrocortisone butyrate	15J12-B03-322394	40	20151028
Caelo	Hydromorphone hydrochloride	13267702	40	0914A-01334
Caelo	Hydromorphone hydrochloride	15393602	60	1516J-01334
Caelo	Hydromorphone hydrochloride	13267702	60	0914A-01334
Caelo	Hydromorphone hydrochloride	15393602	60	1516J-01334
Fagron	Hydromorphone hydrochloride	13E16-N02	40	0914B-01334
Fagron	Hydromorphone hydrochloride	13I25-N05	60	1516I-01334
Fagron	Hydromorphone hydrochloride	15L08-B08-316877	40	1917Q-01334
Fagron	Hydromorphone hydrochloride	13E16-N02	60	0914B-01334
Fagron	Hydromorphone hydrochloride	13I25-N05	60	1516I-01334
Caelo	Ispaghula husk	13238005	40	20130816
Caelo	Juniper, pounded	13367302	40	20131122
Caelo	Kelp, cut	13230805	40	AR-15-FG-007678-01
Caelo	Kelp, cut	15418801	60	AR-17-FG-007505-01
Dr. Behr	L-carnitine hydrochloride	WE11030091	60	from supplier
Dr. Behr	L-carnitine tartrate	WE11060069	40	from supplier
Dr. Behr	L-carnitine tartrate	WE15080050	60	from supplier
Euro OTC	L-carnitine tartrate	1302017-01	40	from supplier
Caelo	Liquorice root, peeled	11351911	40	20120102
Galke	Liquorice root, peeled	22728	40	from supplier
Caelo	Marshmallow root, peeled	13214804	40	20130806
Caelo	Matricaria flower	12337605	40	20121122
Caelo	Methadone hydrochloride	12344818	40	0914E-02949
Caelo	Methadone hydrochloride	15244715	60	1516A-02949
Caelo	Methadone hydrochloride	12344818	60	0914E-02949
Caelo	Methadone hydrochloride	15244715	60	1516A-02949
Fagron	Methadone hydrochloride	13J24-B06	40	0914F-02949
Fagron	Methadone hydrochloride	15E29-B02-313098	60	1516B-02949
Fagron	Methadone hydrochloride	16F24-B02-323183	40	1917Q-02949
Fagron	Methadone hydrochloride	13J24-B06	60	0914F-02949
Fagron	Methadone hydrochloride	15E29-B02-313098	60	1516B-02949
Th. Geyer	Methadone hydrochloride	67033	40	0914G-02949
Th. Geyer	Methadone hydrochloride	67047	40	0914H-02949
Th. Geyer	Methadone hydrochloride	67033	60	0914G-02949
Th. Geyer	Methadone hydrochloride	67047	60	0914H-02949
EDQM	Methylprednisolone acetate	2.0	20	CRS

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Supplier	Substance	Batch	Spectra	Certificate
Flora Apothek...	Mg-Ca-K colamine phos-phate	1000190952	40	from supplier
Th. Geyer	Mg-Ca-K colamine phos-phate	36985	60	from supplier
Th. Geyer	Mg-Ca-K colamine phos-phate	46816	40	from supplier
Th. Geyer	Mg-Ca-K colamine phos-phate	80919	40	from supplier
Fagron	Midazolam	13K05-N01	40	0914E-07393
Fagron	Midazolam	14C12-B31-313222	60	1516A-07393
Fagron	Midazolam	13K05-N01	60	0914E-07393
Fagron	Midazolam	14C12-B31-313222	60	1516A-07393
Caelo	Midazolam hydrochloride	12215811	40	0914E-03538
Caelo	Midazolam hydrochloride	15224602	60	1516B-03538
Caelo	Midazolam hydrochloride	12215811	60	0914E-03538
Caelo	Midazolam hydrochloride	15224602	60	1516B-03538
Fagron	Midazolam hydrochloride	13E22-N09	40	0914F-03538
Fagron	Midazolam hydrochloride	14L23-B04-300245	60	1516A-03538
Fagron	Midazolam hydrochloride	15H04-B03-314396	40	1917R-03538
Fagron	Midazolam hydrochloride	16C14-B12-332469	40	0718E-03538
Fagron	Midazolam hydrochloride	13E22-N09	60	0914F-03538
Fagron	Midazolam hydrochloride	14L23-B04-300245	60	1516A-03538
Fagron	Midazolam hydrochloride	16C14-B12-332469	40	0718E-03538
Caelo	Morphine hydrochloride	13125207	40	0914E-01879
Caelo	Morphine hydrochloride	13349505	40	0914F-01879
Caelo	Morphine hydrochloride	15439404	60	1416R-01879
Caelo	Morphine hydrochloride	16184605	40	1917S-01879
Caelo	Morphine hydrochloride	13125207	60	0914E-01879
Caelo	Morphine hydrochloride	13349505	60	0914F-01879
Caelo	Morphine hydrochloride	15439404	60	1416R-01879
Fagron	Morphine hydrochloride	13G08-N04	40	0914G-01879
Fagron	Morphine hydrochloride	15I09-B08-312694	60	1416Q-01879
Fagron	Morphine hydrochloride	13G08-N04	60	0914G-01879
Fagron	Morphine hydrochloride	15I09-B08-312694	60	1416Q-01879
Th. Geyer	Morphine hydrochloride	67036	40	0914H-01879
Th. Geyer	Morphine hydrochloride	67036	60	0914H-01879
Caelo	Morphine sulfate	12153212	40	0914F-07776
Caelo	Morphine sulfate	11333103	40	0914E-07776
Caelo	Morphine sulfate	15255703	60	1416Q-07776
Caelo	Morphine sulfate	11333103	31	0914E-07776
Fagron	Morphine sulfate	13J07-N04	40	0914G-07776
Fagron	Morphine sulfate	14F02-B06-315405	40	1917Q-07776
Fagron	Morphine sulfate	13J07-N04	60	0914G-07776
Caelo	Myrrh	13108701	40	AR-15-FG-000946-01
Caelo	Orrrh root	11026705	40	20110221
Caelo	Oxycodone hydrochloride	12268908	40	0914E-07734
Caelo	Oxycodone hydrochloride	12034515	40	0914F-07734
Caelo	Oxycodone hydrochloride	12268914	60	1416Q-07734
Caelo	Oxycodone hydrochloride	12268913	60	1416R-07734
Caelo	Oxycodone hydrochloride	12268908	60	0914E-07734
Caelo	Oxycodone hydrochloride	12034515	60	0914F-07734
Caelo	Oxycodone hydrochloride	12268914	60	1416Q-07734
Caelo	Oxycodone hydrochloride	12268913	60	1416R-07734
Caelo	Phenobarbital	12173202	40	0914E-01040
Caelo	Phenobarbital	12173202	60	0914E-01040
Fagron	Phenobarbital	15G07-B06-311718	60	1416Q-01040
Fagron	Phenobarbital	15G07-B06-311718	60	1416Q-01040
Th. Geyer	Phenobarbital	67045	40	0914F-01040
Th. Geyer	Phenobarbital	067056	40	2017A-01040
Th. Geyer	Phenobarbital	67045	60	0914F-01040

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continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Euro OTC	Potassium orotate	1203038V-02	60	from supplier
Euro OTC	Potassium orotate	1203038V-02	40	9757
Euro OTC	Praziquantel	1908004	40	20190830*
Caelo	Siam benzoin	12321312	40	pending
Yino Pharma	Sodium chondroitin sulfate	YN010511806006	40	20180912*
Caelo	Star anise	11314104	30	20111121
Caelo	Stemless carline root	12232802	40	20120822
Klenk	Tormentil	6911B141114	60	AR-15-FG-014020-01
EDQM	Triamcinolone hexacetonide	3.0	40	CRS
Caelo	Zinc stearate	180628	40	20180322*

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Appendix B: Additional validation samples (*Type B*)

It is necessary that spectra also enter the validation which cannot be identified with this model. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *HiperScan GmbH*. They are allocated to the *Type B*. They also include the calibration spectra for other models.

The samples originate from 949 batches. From these 41 790 spectra were recorded. The spectra recorded on independent samples of substances which can be identified with the model are listed respectively in the section *Type B* for the individual substances and do not appear again elsewhere in this list.

Supplier	Substance	Batch	Spectra	Certificate
Fagron	(R,S)-epinephrine chloride	hydro-12H08-N03	40	no certificate available
Fagron	(R,S)-epinephrine chloride	hydro-14A22-B05-291560	60	no certificate available
Fagron	(R,S)-epinephrine chloride	hydro-16H23-B98-325052	40	20160913
Fagron	5-fluorouracil	13F19-N03	40	1402308
Fagron	5-fluorouracil	13F19-N03	60	1608169
Fagron	5-fluorouracil	16D01-U05/3-327376	40	20161117
Fagron	8-quinolinol sulfate monohydrate	12H21-N08	40	20120831
Caelo	Acorus root, natural, cut	12076404	40	20120328
Caelo	Acorus root, peeled	12239001	40	20120905
Caelo	Acorus root, peeled	12295902	40	20121025
Caelo	Agarikon	11024502	40	20110125
Caelo	Agarikon	13130602	48	1405003
Caelo	Agarikon	14190702	60	20140730
Caelo	Agarikon	14190706	60	20140730
Klenk	Agarikon	1061A120312	40	pending
Caelo	Agnus castus fruit	12274003	40	1501649
Caelo	Agnus castus fruit	13193401	40	AR-15-FG-006453-01
Caelo	Agnus castus fruit	15318705	60	pending
Caelo	Agrimony, cut	10325505	45	20101221
Caelo	Agrimony, cut	11374004	40	20120125
Caelo	Alchemilla alpina herb, cut	12147201	40	20120608
Caelo	Alchemilla, cut	12153306	40	20120618
Caelo	Allspice, powdered (spice)	12042703	40	from supplier
Caelo	Almonds, bitter, whole	13220401	40	1406296
Caelo	Aloes, cape, cut	11048808	40	pending
Caelo	Aloes, cape, cut	14087106	60	pending
Caelo	Aloes, cape, powdered	11132115	40	1404400
Caelo	Aloes, cape, powdered	11132115	40	20110520
Caelo	Aloes, cape, powdered	12183008	40	20120802
Fagron	Aluminium chloride hexahydrate, crystalline	12I27-N01	40	20121009
Caelo	Aluminium oxide, aqueous	12163019	40	20120621
Caelo	Aluminium oxide, aqueous	13119121	40	20130503
Fagron	Amiloride hydrochloride	13J08-B04-288620	60	AR-16-FG-008919-01
Fagron	Amiloride hydrochloride	13J08-B04-304547	60	20131024
Fagron	Amiloride hydrochloride	15C25-B05-325653	40	20150410
Fagron	Amiloride hydrochloride	16K07-B02-329114	40	20170104
Fagron	Amiloride hydrochloride	17F02-B06-335953	40	20170630
Caelo	Ammonium chloride	12356101	40	20121206
Euro OTC	Ammonium chloride	1209013-01	40	20120928
Caelo	Ammonium hydrogen carbonate	182108	40	20180926*
Caelo	Amphetamine sulfate	18186907	40	1919M-03361
Caelo	Amphetamine sulfate	16153902	40	2017A-03361

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continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Amphetamine sulfate	18186907	40	1919M-03361
Fagron	Amphetamine sulfate	16A29-B03-324577	40	2017B-03361
Fagron	Amphetamine sulfate	16A29-B03-324577	40	2017B-03361
Th. Geyer	Amphetamine sulfate	067043	40	2017C-03361
abcr GmbH	Amygdalin	1310927	40	from supplier
abcr GmbH	Amygdalin	1310579	40	from supplier
Auropure Life. . .	Amygdalin, bitter almond extract 98%	PA02099-160822	30	from supplier
Caelo	Angelica root	12168701	40	pending
Caelo	Angelica root	12080404	40	1403053
Caelo	Angelica root	12080409	40	20120322
Klenk	Angelica root	6085B120614	40	20120621
Klenk	Angelica root	6085B120614	60	1509356
Caelo	Aniseed	11370301	40	20120117
Caelo	Aniseed	13333903	40	20131018
Klenk	Aniseed	2700A140129	60	20140926
Klenk	Aniseed	2700A160511	60	1708049
Caelo	Aniseed, pounded	12111301	40	20120420
Caelo	Aniseed, pounded	13357101	40	20131202
Caelo	Aniseed, powdered	11306203	40	20111110
Caelo	Apple, cut	11229807	60	from supplier
Caelo	Arnica flower	11285702	40	20111118
Caelo	Arnica flower	11259801	40	20110923
Caelo	Artichoke leaf, cut	12173302	40	20120706
Caelo	Artichoke leaf, cut	13310707	40	20130930
Klenk	Ash bark, cut	0871B110127	60	20110128
Caelo	Ash leaf, cut	11031303	40	20110224
Caelo	Asparagus root, cut	10299010	40	pending
Klenk	Asparagus root, cut	6151B110304	40	1403480
Fagron	Baclofen	18I28-B02-356294	40	20181015
Inresa	Baclofen	206031617/09062017	40	AR-17-FG-018577-01
Caelo	Barberries	11058309	40	pending
Caelo	Barberries	12217109	60	pending
Caelo	Barberries	14057312	60	1508391
Caelo	Barberry root bark, cut	12112601	40	20120430
Fagron	Barbital sodium	15L07-B02-324539	40	2017A-07775
Fagron	Barbital sodium	15L07-B02-324539	40	2017A-07775
Caelo	Barium sulfate	171113	40	20170509*
Caelo	Basil, rubbed	12066404	50	20120321
Caelo	Bean shells, cut	11030601	50	20110221
Caelo	Bearberry leaf, cut	12186502	40	20120705
Caelo	Bentonite	12237603	40	20120810
Caelo	Benzalkonium chloride	16171603	40	20160715
Merck KGaA	Benzoyl peroxide, hydrous	S7012241509	60	20130317
Fagron	Betaine hydrochloride	13H13-N02	40	1402684
Fagron	Betamethasone-17-valerate 1:10 (rice starch)	17F12-B10-34942	40	20170728
Caelo	Betony herb, cut	12007205	40	20120118
Caelo	Betony herb, cut	12007205	60	20120118
Caelo	Bilberry leaf, cut	12140206	40	20120605
Klenk	Birch bark, cut	0561A121121	40	20121127
Caelo	Birch leaf, cut	12193105	40	20120710
Bombastus	Bitter fennel	289870	60	AR-15-FG-008161-01
Caelo	Bitter fennel	12094708	40	pending
Caelo	Bitter fennel	12167102	40	20120705
Caelo	Bitter fennel	13413702	40	1412549
Caelo	Bitter fennel	14376403	60	20150108
Caelo	Bitter fennel	161603	60	20160718*
Caelo	Bitter fennel	17020610	40	1708048
Klenk	Bitter fennel	2880N120418	40	1412547

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continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Klenk	Bitter fennel	2880N120418	40	AR-15-FG-002805-02
Klenk	Bitter fennel	2860A140613	60	AR-15-FG-008160-01
Caelo	Bitter orange flower (petals)	12266605	40	20120907
Caelo	Bitter orange flower (petals)	12266703	40	20120907
Caelo	Bitter orange peel, cut	12067405	40	20120327
Caelo	Black cohosh, cut	10281112	40	20101118
Caelo	Black cohosh, cut	13237901	40	pending
Caelo	Black cohosh, cut	13237903	40	20130812
Caelo	Black cumin seed	11233503	40	1403495
Caelo	Black cumin seed	161157	60	20160708
Caelo	Black mustard seed	12189303	40	1403472
Caelo	Black mustard seed	15120405	60	AR-17-FG-007964-01
Klenk	Black mustard seed	7430A120813	40	AR-15-FG-001050-01
Caelo	Black mustard seed, powdered	13358304	40	pending
Caelo	Black mustard seed, powdered	16051807	60	9887
Klenk	Black mustard seed, powdered	7434A120712	40	AR-15-FG-006711-01
Caelo	Black pepper	11193905	40	20110727
Caelo	Black pepper	12192311	40	1403490
Caelo	Black pepper	13221114	40	20130805
Caelo	Blackberry leaf, cut	11030707	40	20110303
Galke	Blackberry leaf, cut	18060	40	20111021
Caelo	Blackcurrant leaf, cut	12168804	40	20120711
Caelo	Blackcurrants	12272801	40	1403468
Caelo	Blackcurrants	14212502	60	20140829
Caelo	Blackcurrants	14212509	60	20140829
Caelo	Blackthorn flower	12178101	40	20120718
Caelo	Blessed thistle, cut	12038203	40	20120306
Caelo	Blue bottle flower without calyx	10291105	40	pending
Caelo	Blue bottle flower without calyx	13241902	60	AR-15-FG-005838-01
Caelo	Bogbean leaf, cut	12226101	40	20120809
Caelo	Boldo leaf, cut	13367904	40	20131122
Galke	Boldo leaf, cut	19855	40	20120727
Klenk	Boldo leaf, cut	1911A100714	40	20111214
Caelo	Borage herb, cut	11206712	40	20110822
Roth	Brilliant blue R 250 (C.I.42660)	314217301	60	from supplier
Fagron	Bromelain	14F20-B03295501	40	pending
Fagron	Bromelain	14F20-B03295501	60	20140701
Sigma-Aldrich	Bromelain	BCBM1589V	40	from supplier
EDQM	Bromhexine hydrochloride	5.0	40	CRS
Sigma-Aldrich	Bromothymol blue	MKBQ5404V	40	pending
Caelo	Bucho leaf	12034903	40	20120221
Klenk	Buckwheat seed	7510A111011	40	from supplier
Klenk	Buckwheat seed	7510A111011	60	pending
Fagron	Bupivacaine hydrochloride	17E22-B08-345817	40	1905513
Fagron	Bupivacaine hydrochloride	17L05-B04-358735	40	20180111
Caelo	Buprenorphine hydrochloride	12172908	40	0814I-07774
Caelo	Buprenorphine hydrochloride	16143001	40	2017A-07774
Caelo	Buprenorphine hydrochloride	16143001	40	0718E-07774
Caelo	Buprenorphine hydrochloride	16143001	40	1919M-07774

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continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Buprenorphine chloride	hydro- 12172908	60	0814I-07774
Caelo	Buprenorphine chloride	hydro- 16143001	40	2017A-07774
Caelo	Buprenorphine chloride	hydro- 16143001	40	0718E-07774
Caelo	Buprenorphine chloride	hydro- 16143001	40	1919M-07774
Caelo	Burdock root, cut	11100801	40	20110523
Caelo	Burnet root	12027410	40	20120206
Caelo	Burnet root	12027407	40	20120206
Caelo	Burnet root	12024406	40	20120206
Fagron	Caffeine citrate	12C16-N03	40	1403477
Fagron	Caffeine citrate	15A05-B03-302746	60	20150115
Fagron	Caffeine citrate	15A05-B03-318006	40	20150115
Fagron	Caffeine citrate	15A05-B03-318006	40	20150115
Fagron	Caffeine citrate	15A05-B03-302746	40	20150115
Gatt-Koller	Caffeine citrate	1783/05140715	60	AR-15-FG-014994-01
Gatt-Koller	Caffeine citrate	4065/11164916	40	20161130
Euro OTC	Calcium carbonate, light	1611008-01	40	20161201
Caelo	Calcium chloride dihydrate	182411	35	20181022*
Th. Geyer	Calcium colamine phosphate	36986	40	from supplier
Caelo	Calcium hydrogen phosphate, powdered	181117	40	20180528*
Fagron	Calcium hydroxide	13E22-N07	20	20130626
Caelo	Calcium oxide	182244	39	20181106*
Caelo	Calcium sulfate dihydrate	163363	40	20161214*
Caelo	Calcium sulfate hemihydrate	153451	30	20151103*
Caelo	Calendula flower	11221404	40	20110930
Klenk	Calendula flower	1241B130321	40	20130408
Caelo	Calendula flower, cut	11187605	40	20110930
Caelo	Campeche wood	11074105	40	from supplier
Caelo	Caraway fruit	11003217	40	20110209
Caelo	Caraway fruit	13397104	40	AR-15-FG-001526-01
Caelo	Caraway fruit	13397104	60	AR-15-FG-001527-01
Caelo	Caraway fruit	13306006	60	AR-16-FG-000540-03
Caelo	Caraway fruit	15097115	60	AR-17-FG-006649-01
Caelo	Caraway fruit, pounded	12116904	40	20120503
Caelo	Caraway fruit, pounded	13367101	40	20130503
Caelo	Caraway fruit, pounded	14358801	60	AR-15-FG-014914-01
Caelo	Caraway fruit, pounded	16073201	60	AR-17-FG-006648-01
Caelo	Carbachol	11150302	31	1401147
Caelo	Cardamom fruit	11309107	40	20111111
Caelo	Cardamom fruit	13260504	40	20130906
Klenk	Cardamom, excorticated, powdered (spice)	2765A130524	60	AR-15-FG-015285-01
Caelo	Carnauba wax	170903	40	20170512*
Caelo	Carnauba wax	183330	40	20190114*
Lycored corp.	Caromix	CMX-LLCV-011401	40	20140131
Caelo	Castoreum, powdered	12137409	40	1402590
Caelo	Castoreum, powdered	13410403	40	20131231
Caelo	Castoreum, powdered	13410403	40	20131231
Klenk	Celery fruit	7140A130625	40	1405177
Klenk	Celery fruit	7140A131122	60	20131204
Caelo	Celery root, cut	10270002	40	20101006
Klenk	Celery root, cut	6091A110110	40	1410177
Caelo	Centaury, cut	11097602	40	20110428

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Klenk	Chelidonium majus herb, cut	3731K120904	40	20120920
Klenk	Chervil, rubbed	3721A100329	40	20111128
Caelo	Chickweed, cut	13040502	40	1403482
Caelo	Chickweed, cut	13254411	40	1412550
Caelo	Chicory herb, cut	12034303	60	20120228
Caelo	Chicory herb, cut	12354302	100	20121211
Fagron	Chlorhexidine dihydrochloride	14A09-B03-290724	40	AR-15-FG-012308-01
Fagron	Chlorhexidine dihydrochloride	16C11-B02-324203	40	20160412
Fagron	Chlorhexidine dihydrochloride	16C11-B02-322510	40	20160412
Fagron	Chlorhexidine dihydrochloride	16C11-B02-329881	40	20160412
Fagron	Chlorobutanol hemihydrate	14A06-B31-290310	60	1412458
Audor	Chlorprothixene hydrochloride	AP05061117C	40	1810394
Audor	Chlorprothixene hydrochloride	AP04120418C	40	20180925
Euro OTC	Cholecalciferol dry concentrate	1210051-01	40	1403341
Euro OTC	Cholecalciferol dry concentrate	1304016-02	40	20130425
Euro OTC	Cholecalciferol dry concentrate	1502021-01	60	20150309
Euro OTC	Cholecalciferol dry concentrate	1508032	60	20150901*
Euro OTC	Cholecalciferol dry concentrate	1602019	40	20160307*
Euro OTC	Cholecalciferol dry concentrate	1608002	40	20160824*
Euro OTC	Cholecalciferol dry concentrate	1701053	40	20170208*
Euro OTC	Cholecalciferol dry concentrate	1707027	40	20171020*
Euro OTC	Cholecalciferol dry concentrate	1802014	40	20180223*
Euro OTC	Cholecalciferol dry concentrate	1801038	40	20180206*
Euro OTC	Cholecalciferol dry concentrate	1806003	40	20180618*
Euro OTC	Cholecalciferol dry concentrate	1812010	40	20190114*
Euro OTC	Cholecalciferol dry concentrate	1901050	40	20190221*
Euro OTC	Cholecalciferol dry concentrate	1906009	40	20190619*
Euro OTC	Chromium yeast 0.2%	L1303028-01	40	1403474
Euro OTC	Chromium yeast 0.2%	L1406030-02	60	20140807
Fagron	Cinchocaine hydrochloride	12F25-N10	40	1401148
Fagron	Cinchocaine hydrochloride	13G24-N05	40	20130826
Caelo	Cinchona bark, cut	11238512	40	1403463
Caelo	Cinchona bark, cut	13031007	40	20130207
Caelo	Cinchona bark, cut	14009304	40	AR-15-FG-007677-01
Caelo	Cinchona bark, cut	15301903	60	AR-17-FG-007831-01
Caelo	Cinnamon rods (Ceylonese Cinnamon)	13241807	40	20130905
Caelo	Cinnamon, cut	12309902	40	pending
Caelo	Cinnamon, cut	13304414	40	20130912

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Cinnamon, cut	14175010	60	1505349
Caelo	Cinnamon, cut	16114401	60	1704441
Fagron	Cinnarizine	11L22-N13	40	20120104
Fagron	Cinnarizine	13H01-N07	40	1402306
Fagron	Cinnarizine	14D09-B01-294702	60	AR-16-FG-008930-01
Klenk	Cleavers goosegrass, cut	4731B110809	40	20110930
Caelo	Clindamycin-2-dihydrogen phosphate	13166605	40	1403485
Caelo	Clindamycin-2-dihydrogen phosphate	13166605	40	20130624
Caelo	Clindamycin-2-dihydrogen phosphate	14257305	60	AR-15-FG-015412-01
Caelo	Clindamycin-2-dihydrogen phosphate	15435801	60	AR-16-FG-009129-01
Caelo	Clindamycin-2-dihydrogen phosphate	163265	40	20161214*
Caelo	Clindamycin-2-dihydrogen phosphate	16326504	40	AR-17-FG-022557-01
Caelo	Clindamycin-2-dihydrogen phosphate	172964	40	20171109*
Caelo	Clindamycin-2-dihydrogen phosphate	191224	40	20190523*
Caelo	Clindamycin-2-dihydrogen phosphate	14257305	60	AR-15-FG-015412-01
Caelo	Clindamycin-2-dihydrogen phosphate	15435801	60	20160122
Caelo	Clindamycin-2-dihydrogen phosphate	163265	40	20161214*
Fagron	Clobetasol-17-propionate 1:10 (rice starch)	13E16-N01	40	20130619
Caelo	Clove	12095805	40	pending
Caelo	Clove	16207804	60	1708676
Klenk	Clove	1260A150916	40	1708050
Klenk	Clove, powdered (spice)	1264B141007	60	AR-15-FG-014858-01
Caelo	Cocaine hydrochloride	16142710	40	1917T-01278
Caelo	Cocaine hydrochloride	18266104	40	1919M-01278
Caelo	Cocaine hydrochloride	17003902	40	1917S-01278
Caelo	Cocaine hydrochloride	16142710	40	1917T-01278
Caelo	Cocaine hydrochloride	18266104	40	1919M-01278
Fagron	Cocaine hydrochloride	14H27-B03-304551	40	1917R-01278
Fagron	Cocaine hydrochloride	18J01-B07-353630	40	1919I-01278
Fagron	Cocaine hydrochloride	16B11-B05-323386	40	1917Q-1278
Fagron	Cocaine hydrochloride	14H27-B03-304551	40	1917R-01278
Fagron	Cocaine hydrochloride	18J01-B07-353630	40	1919I-01278
Fagron	Codeine monohydrate	12C05-N05	40	0814I-01280
Fagron	Codeine monohydrate	12C05-N05	60	0814I-01280
Caelo	Codeine phosphate hemihydrate	16349702	40	2017C-01279
Caelo	Codeine phosphate hemihydrate	16169807	40	2017B-01279
Caelo	Codeine phosphate hemihydrate	18187906	40	1919M-01279
Caelo	Codeine phosphate hemihydrate	16349702	40	2017C-01279
Caelo	Codeine phosphate hemihydrate	16169807	40	2017B-01279
Caelo	Codeine phosphate hemihydrate	18187906	40	1919M-01279
Fagron	Codeine phosphate hemihydrate	16E17-B05-324109	40	2017A-01279

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Th. Geyer	Codeine phosphate hemihydrate	067054	40	2017D-01279
Caelo	Colophony	12301410	60	AR-15-FG-016314-01
Caelo	Colophony	15186804	60	AR-16-FG-005931-01
Caelo	Colophony	161332	40	20160510*
Caelo	Colophony	173014	40	20180102*
Caelo	Colophony	173014	40	20180102*
Caelo	Colophony	192081	40	20190731*
Caelo	Colophony	191664	40	20190701*
Klenk	Comfrey root	6244B130624	40	20130625
Caelo	Common wormwood herb, cut	12016705	40	20120131
Caelo	Copper (II) sulfate pentahydrate	162409	40	20160825*
Caelo	Coriander	12080904	40	pending
Caelo	Coriander	13299403	40	1412548
Caelo	Coriander	16010212	60	AR-17-FG-015965-01
EDQM	Cortisone acetate	6.0	20	CRS
Caelo	Cottonwood bud	12027505	40	20120131
Klenk	Cottonwood bud, pounded	3266B130826	40	1410178
Klenk	Cottonwood bud, pounded	3266B150624	60	20150701
Caelo	Couch grass rhizome, cut	12186702	40	20120629
Caelo	Cowberry leaf, cut	11334302	40	20111129
Kreatin.de GmbH	Creatine	300331	50	1405615
Caelo	Cumin	11378308	30	20120124
Klenk	Cumin, powdered	2824B121001	40	20121009
Euro OTC	Curcuma extract 95%	L1408013	60	20140815
Fagron	Cyproheptadine hydrochloride	16K07-B01-350645	40	1906179
Euro OTC	Cysteine hydrochloride monohydrate	1304019-01	40	20130517
Euro OTC	Cysteine hydrochloride monohydrate	1507006	60	20150713*
Euro OTC	Cysteine hydrochloride monohydrate	1510015	60	20151112*
Euro OTC	Cysteine hydrochloride monohydrate	1603018	40	20160419*
Euro OTC	Cysteine hydrochloride monohydrate	1701012	40	20170207*
Euro OTC	Cysteine hydrochloride monohydrate	1706023	40	20170721*
Euro OTC	Cysteine hydrochloride monohydrate	1807010-01	40	20180808
Euro OTC	Cysteine hydrochloride monohydrate	1901012	40	20190206*
VMP Chemiekon...	D-(+)-glucosamine hydrochloride	144212943	40	20140402
Euro OTC	D-(+)-mannose	L1111005-02	40	1405612
Euro OTC	D-(+)-mannose	L1111005-02	40	20111130
Euro OTC	D-(+)-mannose	L1503016-01	60	20150319
Caelo	Daisy flower	11068306	40	20110323
Caelo	Damiana leaf, cut	11026608	40	20110221
Caelo	Dandelion herb without root, cut	11217109	40	20110824
Caelo	Dandelion root, cut	12363102	40	1403708
Caelo	Dandelion root, cut	13329701	40	20131017
Caelo	Dandelion root, cut	13329708	40	1411089
Klenk	Dandelion root, cut	6621B151029	60	AR-17-FG-007535-01
Caelo	D-Camphor	162354	40	20160809*
Caelo	D-Camphor	190097	40	20190124*

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Fagron	Deoxycholic acid	14A02-B32-303429	60	AR-16-FG-004648-01
Fagron	Deoxycholic acid	14A02-B32-303429	40	from supplier
Roth	Deoxycholic acid sodium salt ($\geq 98\%$ for biochemistry)	084181622	40	1405618
Roth	Deoxycholic acid sodium salt ($\geq 98\%$ for biochemistry)	154212633	60	20140327
Roth	Deoxycholic acid sodium salt ($\geq 98\%$ for biochemistry)	385212633	60	20140327
Caelo	Devil's claw root	12031806	40	20120222
Caelo	Devil's claw root	13298202	40	20130926
Euro OTC	Devil's claw root extract 4:1	1210003-02	40	1707472
Euro OTC	Devil's claw root extract 4:1	1210003-02	40	20151102
Euro OTC	Devil's claw root extract 4:1	1210003-02	40	20151102
Fagron	Dexamethasone 1:10 (rice starch)	18C13-B06-348239	40	20180502
Sigma-Aldrich	Dexamethasone isonicotinate	Y0000538	40	CRS
Sigma-Aldrich	Dexamethasone sodium phosphate	LRAC1690	40	CRS
Fagron	Dexamphetamine sulfate	16F09-B02-328352	40	2017A-03582
Fagron	Dexamphetamine sulfate	16D20-B01-321049	40	2017B-03582
Fagron	Dexamphetamine sulfate	16F09-B02-328352	40	2017A-03582
Caelo	Dihydrocodeine hydrogen tartrate	16106209	40	2017C-03065
Caelo	Dihydrocodeine hydrogen tartrate	15295910	40	2017B-03065
Caelo	Dihydrocodeine hydrogen tartrate	18115205	40	1919M-03065
Caelo	Dihydrocodeine hydrogen tartrate	16106209	40	2017C-03065
Caelo	Dihydrocodeine hydrogen tartrate	15295910	40	2017B-03065
Caelo	Dihydrocodeine hydrogen tartrate	18115205	40	1919M-03065
Fagron	Dihydrocodeine hydrogen tartrate	14K26-B04-306298	60	1516I-03065
Fagron	Dihydrocodeine hydrogen tartrate	15F18-B07-323388	40	2017A-03065
Th. Geyer	Dihydrocodeine hydrogen tartrate	067052	40	2017D-03065
Caelo	Dill fruit	12289901	40	1403464
Caelo	Dill fruit	12342906	40	20121206
Caelo	Dill fruit	14018705	60	pending
Klenk	Dill fruit	2680A170222	60	20170308
Caelo	Dill herb, cut	11295103	40	20111103
Caelo	Dill herb, cut	11295107	40	pending
Caelo	Dill herb, cut	13007602	40	1402204
Caelo	Dill herb, cut	13007610	40	20130208
abcr GmbH	Dimercaptosuccinic acid	1005874	39	from supplier
Safic-Alcan	Dimercaptosuccinic acid	20180130	40	from supplier
Fagron	Diphenylcyclopropenone	12L17-N07	40	1407599
Fagron	Diphenylcyclopropenone	13I26-N12	40	1504598
Fagron	Diphenylcyclopropenone	13I26-N12	35	20130920
Fagron	Diphenylcyclopropenone	15J12-B01-316620	60	9341
Fagron	Diphenylcyclopropenone	16F02-B10-329708	40	1902476
Fagron	Diphenylcyclopropenone	16F02-B10-326265	40	20160822
Fagron	Diphenylcyclopropenone	18I03-B04-356833	40	20181121

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Sand 12 GmbH	D-ribose	L201211720	35	from supplier
Fagron	Drofenine hydrochloride	13I09-N05	40	20130524
Fagron	Drofenine hydrochloride	15G01-B04-323028	40	20150709
Fagron	Drofenine hydrochloride	15G01-B04-330979	40	AR-17-FG-015434-02
Fagron	Drofenine hydrochloride	15G01-B04-330979	40	20150709
Fagron	Drofenine hydrochloride	18A18-B99-345993	40	20180308
Caelo	Dry beads Caelo orange	11005804	40	from supplier
Caelo	Dry beads Caelo orange	12382203	40	from supplier
Caelo	Echinacea pallida root, cut	12244501	40	20120817
Caelo	Echinacea pallida root, cut	14120602	40	20140417
Fagron	Econazole nitrate	12H08-N02	40	1312442
Fagron	Econazole nitrate	11F09-N16	40	20110606
Fagron	Econazole nitrate	12I06-B40-306925	40	AR-16-FG-011359-01
Fagron	Econazole nitrate	14G22-B07-327805	40	20140804
Fagron	Econazole nitrate	12I06-B40-306925	40	20140127
Euro OTC	EDTA calcium disodium	1705029	40	20170626*
Euro OTC	EDTA calcium disodium	1807024	40	20180725*
Euro OTC	EDTA calcium disodium	1901028	40	20190218*
Euro OTC	EDTA calcium disodium	1910014	40	20191119*
Caelo	Elder berries	12267807	40	1403466
Caelo	Elder berries	13367704	40	1410179
Klenk	Elder berries	3010A120202	40	pending
Caelo	Elder flower, rubbed	12221902	40	20120821
Klenk	Elder leaf, cut	2321B130221	60	20130226
Caelo	Elecampane rhizome, cut	12113303	40	20120427
Klenk	Elecampane rhizome, cut	6341B120611	40	20120620
Caelo	Eleutherococcus, cut	10381814	30	20110113
Caelo	Elm bark, cut	10347205	60	20101223
Caelo	Emser salt, artificial	181633	40	20180621*
Caelo	Equisetum stem, cut	10375515	40	20110114
Fagron	Ergotamine tartrate	13H02-N01	100	20120412
Fagron	Ergotamine tartrate	13I24-B10-288648	50	20131024
Fagron	Ergotamine tartrate	13I24-B10-288650	60	20131024
Fagron	Ergotamine tartrate	15B16-B05-308418	45	9384
Fagron	Ergotamine tartrate	15B16-B05-308417	40	20150302
Fagron	Ergotamine tartrate	15B16-B05-308418	45	9384
Fagron	Ergotamine tartrate	15B16-B05-308417	40	20150302
Roth	Esculin	155206581	60	20131022
Fagron	Ethyl hydrogen fumarate	14C12-B07-292760	60	1410436
Fagron	Ethyl hydrogen fumarate	14C12-B07-292760	60	20140417
Euro OTC	Ethyl hydrogen fumarate magnesium	1306014-01	60	20130805
Euro OTC	Ethyl hydrogen fumarate magnesium	1510006	60	20151030*
Euro OTC	Ethyl hydrogen fumarate magnesium	1601010	60	20160114*
Euro OTC	Ethyl hydrogen fumarate magnesium	1510006-01	40	AR-18-FG-000547-01
Fagron	Ethyl hydrogen fumarate magnesium	13G10-N01	60	1411091
Caelo	Eucalyptus leaf, cut	11307706	40	20111111
Klenk	Euphrasy herb, cut	3871B100713	40	20100721
Fagron	Fentanyl citrate	16E26-B01-525360	40	2017A-03686
Fagron	Fentanyl citrate	16E26-B01-525360	40	2017A-03686
Caelo	Fenugreek	11313204	40	20111122
Caelo	Fenugreek, powdered	12149605	40	20120629
Caelo	Fenugreek, powdered	15308704	60	AR-17-FG-006625-01
Klenk	Fenugreek, powdered	7264B130205	40	1408080
Klenk	Fenugreek, powdered	7264A151001	60	AR-16-FG-014493-01
Caelo	Flax weed herb, cut	13007505	40	1403462

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Flax weed herb, cut	14005309	60	20140203
Audor	Fluconazole	AP061502911F	60	AR-16-FG-008733-01
Audor	Fluconazole	AP061502911F	40	AR-16-FG-014225-01
Audor	Fluconazole	AP061502911F	40	20150821
Audor	Fluconazole	APAFLNC0217023F	40	20170421
Audor	Fluconazole	AP061502911F	60	20150821
Audor	Fluconazole	AP061502911F	40	20150821
Audor	Fluconazole	AP061502911F	40	20150821
Caelo	Frangula bark, cut	12185901	40	20120710
Caelo	Frankincense	12120005	40	1402495
Caelo	Frankincense	13112801	40	20130503
Euro OTC	Frankincense extract 80%	1308020-01	60	8958
Euro OTC	Frankincense extract 80%	1602008	60	20160215*
Euro OTC	Frankincense extract 80%	1602008	60	20160215*
Euro OTC	Frankincense extract 80%	1611023-01	60	9889
Caelo	Fraxinella root, cut	10189103	40	20100804
Caelo	Fraxinella root, cut	11314705	40	pending
Caelo	Fraxinella root, cut	11314705	80	20111115
Caelo	Fraxinella root, cut	14110802	60	20140428
Caelo	Fumitory, cut	12103402	40	20120425
Caelo	Galangal root	12125001	40	20120516
Caelo	Galangal root	11375904	40	20120109
Caelo	Galangal root	12330305	40	1403491
Caelo	Galangal root	11375909	40	1403324
Caelo	Galangal root	12330308	40	20121203
Caelo	Galangal root	14159504	60	1511617
Klenk	Galeopsis herb, cut	3911A090219	40	20120426
Caelo	Garden violet, cut	10292002	40	pending
Caelo	Garden violet, cut	13038703	40	1403481
Caelo	Garden violet, cut	13232103	40	20130821
Caelo	Gentian root, cut	12244603	40	20120914
Caelo	Gentian root, powdered	12007103	50	1403630
Caelo	Gentian root, powdered	12007106	40	20120117
Caelo	Gentian root, powdered	13410503	40	1508394
Caelo	Ginger, peeled	12180601	40	20120730
Caelo	Ginger, peeled	14120701	40	20140516
Caelo	Ginger, peeled	13321904	40	20131016
Klenk	Ginger, peeled, powdered	6954B140724	60	AR-15-FG-014915-01
Klenk	Ginger, peeled, powdered	6954B150325	60	1606616
Klenk	Ginger, peeled, powdered	6954B160429	60	1704440
Klenk	Ginger, peeled, powdered	6954B170127	60	1708675
Caelo	Ginkgo extract	12192505	40	1403672
Caelo	Ginkgo leaf, cut	12151703	40	20120613
Caelo	Ginkgo leaf, cut	13340904	40	1411088
Caelo	Ginkgo leaf, cut	13340907	60	20131028
Caelo	Ginkgo leaf, cut	16281501	60	1708047
Caelo	Ginseng root	12080208	40	20120329
Caelo	Ginseng root	11349206	40	20111227
Caelo	Ginseng root	13341008	40	20131029
Caelo	Ginseng root	13237805	40	20130816
abcr GmbH	Glycyrrhizic acid	1222024	40	from supplier
Klenk	Goat's rue, cut	3901C110905	40	20111005
Klenk	Greek mountain herb, cut	4511K130314	40	20130402
Klenk	Green tea	5100A100611	40	20120126
Euro OTC	Griffonia seed extract	1810009	40	20181025*
Caelo	Guaiacum wood, cut	11352001	40	1406340
Caelo	Guaiacum wood, cut	11352012	40	20111222
Caelo	Guaiacum wood, cut	13343802	40	20131113
Caelo	Hamamelis bark, cut	12361301	40	20121213
Caelo	Hamamelis bark, cut	12361303	40	20121213

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Hamamelis leaf, cut	10102915	40	20100517
Caelo	Hamamelis leaf, cut	13269902	40	1405176
Caelo	Hamamelis leaf, cut	13269904	40	20130924
Caelo	Hawthorn flower	10157201	40	20100701
Caelo	Hawthorn flower	13010403	40	20130130
Caelo	Hawthorn fruit	11183010	40	20110701
Caelo	Hawthorn fruit	11278205	30	20111025
Caelo	Hawthorn leaf with flower, cut	10273515	40	20101028
Caelo	Hawthorn leaf with flower, cut	10273513	40	20101028
Caelo	Hawthorn leaf with flower, cut	13276706	40	20130927
Galke	Hawthorn leaf with flower, cut	21126	40	20121109
Caelo	Heather flower, rubbed	10270508	40	20101018
Caelo	Heather, cut	11011209	40	20110218
Caelo	Heavy alkaline bismuth sub-nitrate	181942	40	20181010*
Euro OTC	Heavy magnesium oxide	1709011-02	40	20170915
Caelo	Henna powder	12122302	40	from supplier
Caelo	Henna powder	12267304	40	from supplier
Fagron	Homatropine hydrobromide	18L11-B03-356938	40	1905511
Caelo	Hop strobile	12008305	40	20120213
Caelo	Hop strobile	12221802	40	20120817
Caelo	Horse chestnut leaf, cut	11063503	40	20110315
Fagron	Hydrocortisone butyrate	13I26-N01	60	AR-15-FG-000944-01
Fagron	Hydrocortisone butyrate	14D23-B01-296716	60	20140509
Fagron	Hydrocortisone butyrate	13I26-N01	60	20130920
Fagron	Hydrocortisone butyrate	16F20-B05-323903	40	20160805
Fagron	Hydrocortisone butyrate	15J12-B03-322394	40	20151028
Fagron	Hydrocortisone butyrate	16J21-B01-333229	40	20161206
Fagron	Hydrocortisone butyrate	16J21-B01-333229	40	20161206
Fagron	Hydrocortisone butyrate	14D23-B01-296716	48	20140509
Fagron	Hydrocortisone butyrate	13I26-N01	45	20130920
Fagron	Hydrocortisone butyrate	16F20-B05-323903	20	20160805
Fagron	Hydrocortisone butyrate	15J12-B03-322394	25	20151028
Fagron	Hydrocortisone butyrate	15J12-B03-322394	22	20151028
Fagron	Hydrocortisone butyrate	16J21-B01-333229	37	20161206
Fagron	Hydrocortisone butyrate	16J21-B01-333229	36	20161206
EDQM	Hydrocortisone hydrogen succinate	3.0	40	CRS
Caelo	Hydromorphone chloride	16123804	40	1917R-01334
Caelo	Hydromorphone chloride	18316002	40	1919M-01334
Caelo	Hydromorphone chloride	16123804	40	1917R-01334
Caelo	Hydromorphone chloride	18316002	40	1919M-01334
Fagron	Hydromorphone chloride	17F01-B01-337510	40	1919I-01334
Fagron	Hydromorphone chloride	15L08-B08-316877	40	1917Q-01334
Fagron	Hydromorphone chloride	17F01-B01-337510	40	1919I-01334
Caelo	Hydroxyethylcellulose (apparent viscosity 10000 mPas)	181131	40	20180612*

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Hydroxyethylcellulose (apparent viscosity 10000 mPas)	191675	40	20190716*
Caelo	Hydroxyethylcellulose (apparent viscosity 15000 mPas)	190174	40	20190411*
Caelo	Iceland moss, cut	12187106	40	1403493
Caelo	Iceland moss, cut	13350803	40	20131114
Fagron	Indigo carmine	13K12-N01	40	1601099
Spinnrad	Inulin	1112300433	40	from supplier
Caelo	Iodine	181635	40	20180704*
Euro OTC	Iron (II) gluconate	1805025	40	20180604*
Caelo	Iron (II) sulfate heptahydrate	11340509	40	1401568
Caelo	Iron (III) chlorid hexahydrate	12354703	40	1401391
Caelo	Iron (III) sulfate hydrate	170991	40	20170523*
EDQM	Isoconazole	1.1	40	CRS
EDQM	Isoconazole nitrate	1.1	40	CRS
Caelo	Isomalt	170812	40	20170421*
Caelo	Ispaghula husk	12148103	40	20120628
Caelo	Ispaghula seed	11185807	40	20110727
Caelo	Ivy leaf, cut	11229505	40	20110829
Caelo	Ivy leaf, cut	13276304	40	20130913
Caelo	Jasmine flower	12143201	40	20120606
Caelo	Java tea, cut	12225702	40	20120809
Caelo	Java tea, cut	13258805	40	20130826
Klenk	Java tea, cut	2221B110718	40	20120605
Caelo	Juniper	12028609	40	20120207
Caelo	Juniper	13267210	40	20130828
Caelo	Juniper, pounded	12278903	40	1405296
Klenk	Juniper, powdered	2894B130320	40	1411362
Klenk	Juniper, powdered	2894B150922	60	1704439
Caelo	Kaolin, heavy	11350124	40	20120102
Caelo	Kaolin, red, powdered	12093503	40	from supplier
Inresa	Ketoprofen	F1300183	60	AR-15-FG-009572-01
Inresa	Ketoprofen	F1300182	60	20150617
Caelo	Kidney vetch, coarsely rubbed	10249206	40	20100928
Caelo	Knotgrass, cut	14079304	40	20140402
Klenk	Knotgrass, cut	4301A120912	40	20120924
Caelo	Ladys bedstraw herb, cut	11265103	40	20111006
Klenk	Ladys bedstraw herb, cut	3921B101012	40	20111216
Euro OTC	L-alanine	1710009	40	20171018*
Euro OTC	L-alanine	1601033-01	40	20160225
Caelo	Lapacho wood, cut	12239305	40	20120831
Caelo	Lapis Pumicis	180533	40	20180222*
Caelo	Laurel leaf	12299103	40	20121108
Klenk	Laurel leaf, powdered	2124A110329	40	1411032
Klenk	Laurel leaf, powdered	2124A110329	60	20140310
Caelo	Lavender flower	12088003	60	20120411
Caelo	Lavender flower	13336005	40	from supplier
Euro OTC	L-carnitine tartrate	1708023	40	20170907*
Pharmorgana	L-carnitine tartrate	1000160672	40	from supplier
Pharmorgana	L-carnitine tartrate	1000170113	40	from supplier
Caelo	Lemon peel, cut	12217402	40	20120823
Caelo	Lemon verbena leaf, cut	12137505	40	20120605
Caelo	Lemon verbena leaf, cut	12137503	40	20120605
Flora Apothek. ...	Levamisole hydrochloride	LV17203	40	from supplier
Flora Apothek. ...	Levamisole hydrochloride	LV19305	40	from supplier

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Lime flower, cut	11086305	55	20110420
Caelo	Linseed	12186902	60	pending
Caelo	Linseed	12092102	60	20120402
Caelo	Linseed	13296703	40	20131008
Caelo	Linseed	13412801	40	20140113
Caelo	Liquorice root, peeled	12227101	40	20120813
Caelo	Liquorice root, peeled	12227106	40	20120813
Caelo	Liquorice	13068904	40	20130315
Caelo	Liquorice	14050601	60	from supplier
Caelo	Liquorice	13180904	60	pending
Caelo	Liquorice root, natural, cut	12267103	40	20120917
Caelo	Locust bean gum, powdered	10376516	40	20110106
Caelo	Locust bean gum, powdered	13379403	40	from supplier
Caelo	Lovage root, cut	11181609	40	20110629
Fagron	Macrogols 6000 powder	14C11-B01-296014	60	20140324
Fagron	Macrogols 6000 powder	14J17-B01-309247	60	20141027
Fagron	Macrogols 6000 powder	14J17-B01-309247	60	AR-16-FG-011486-01
Fagron	Mafenide acetate	15J20-B05-342526	40	20151221
Caelo	Magnesium hydrogen phosphate trihydrate	12181911	40	20120716
Fagron	Magnesium aspartate dihydrate	15I24-B89-313231	60	AR-16-FG-008660-03
Fagron	Magnesium aspartate dihydrate	15I24-B89-313231	60	20151016
Fagron	Magnesium aspartate dihydrate	17C21-B05-333111	40	20170412
Fagron	Magnesium aspartate dihydrate	18D23-B01-350069	40	20180625
Caelo	Magnesium carbonate, heavy, alkaline	182282	40	20180906*
Euro OTC	Magnesium carbonate, light, basic	1711011-01	40	20171116
Euro OTC	Magnesium chloride hexahydrate	1802023-01	40	20180223
Caelo	Magnesium hydroxide	16253301	30	20160921
Caelo	Magnesium oxide, light	180818	40	20180322*
Caelo	Magnesium peroxide 22-28%	190555	40	20190306*
Caelo	Magnesium sulfate heptahydrate	13340814	60	20131024
Caelo	Magnesium sulfate, dried	172990	40	20171129*
Euro OTC	Magnesium trisilicate	1608024-01	40	20160908
Bombastus	Maize style, cut	274920	40	66662
Caelo	Maize style, cut	10325906	40	20101217
Caelo	Maize style, cut	13381501	40	20140103
Klenk	Maize style, cut	5581A111206	40	20111214
Caelo	Male speedwell wort, cut	12162503	40	20120703
Caelo	Mallow flower, cut	12187405	40	20120719
Caelo	Mallow leaf, cut	12153403	40	20120614
Inresa	Maltodextrin	R1503902	60	AR-15-FG-008821-01
Inresa	Maltodextrin	R1600014	60	20160202
Caelo	Manganese sulfate monohydrate	171648	40	20170714*
Caelo	Manna, cut	11308907	60	pending
Caelo	Manna, cut	13127007	40	pending
Caelo	Manna, powdered	11308807	40	1403534
Caelo	Manna, powdered	14001401	40	20140115
Caelo	Marian thistle fruit	11126703	40	20110608
Caelo	Marian thistle fruit	13342002	40	from supplier
Caelo	Marian thistle herb, cut	10365601	40	20110111
Caelo	Marshmallow leaf, cut	12328206	40	20121114

continued on the next page

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Supplier	Substance	Batch	Spectra	Certificate
Caelo	Marshmallow root, peeled	11101905	40	20110406
Caelo	Masterwort root, cut	12101804	60	20120405
Caelo	Masterwort root, cut	13341204	40	20131030
Caelo	Maté leaf, cut	11091707	40	20110428
Caelo	Maté leaf, cut	13118004	40	20130506
Galke	Maté leaf, cut	21684	40	from supplier
Caelo	Matricaria flower	12294804	40	20121113
Caelo	Matricaria flower for bathing	12115805	40	from supplier
Caelo	Meadowsweet flower, rubbed	12275701	40	20121023
Klenk	Meadowsweet herb, cut	4541A120313	60	20120327
Caelo	Medical coal	181885	40	20180813*
EDQM	Medroxyprogesterone acetate	3.0	40	CRS
Caelo	Melissa leaf, cut	12032318	40	20120302
Caelo	Melissa leaf, cut	13214713	40	20130806
Galke	Melissa leaf, cut	22218	40	from supplier
Klenk	Melissa leaf, cut	2161A090630	130	20120328
Klenk	Melissa leaf, cut	2161A121029	55	20121113
Caelo	Methadone hydrochloride	16135309	40	1917R-02949
Caelo	Methadone hydrochloride	18132413	40	1919Q-02949
Caelo	Methadone hydrochloride	16135309	40	1917R-02949
Caelo	Methadone hydrochloride	18132413	40	1919Q-02949
Fagron	Methadone hydrochloride	18G02-B02-355990	40	1919I-02949
Fagron	Methadone hydrochloride	16F24-B02-323183	40	1917Q-02949
Fagron	Methadone hydrochloride	18G02-B02-355990	40	1919I-02949
Th. Geyer	Methadone hydrochloride	067055	40	1917S-02949
Th. Geyer	Methadone hydrochloride	067055	40	1917S-02949
EDQM	Methylprednisolone hydro-gen succinate	3.0	40	CRS
Caelo	Methylrosanilinium chloride	12276308	40	1509299
Fagron	Methylrosanilinium chloride	13G03-N11	40	20130813
Fagron	Methylrosanilinium chloride	13H28-N03	60	20130625
Fagron	Methylrosanilinium chloride	13H28-N03	60	AR-15-FG-004742-01
EDQM	Metronidazole benzoate	1.3	40	CRS
Th. Geyer	Mg-Ca-K colamine phosphate	54610	40	from supplier
Th. Geyer	Mg-Ca-K colamine phosphate	54610	40	from supplier
Dr. K. Hollbo...	Miconazole	029C064	40	20190415
Fagron	Midazolam	16J03-B09-326963	40	1917Q-07393
Fagron	Midazolam	17J16-B01-342518	40	1919I-07393
Fagron	Midazolam	16J03-B09-326963	30	1917Q-07393
Fagron	Midazolam	17J16-B01-342518	40	1919I-07393
Caelo	Midazolam hydrochloride	15224611	40	1917S-03538
Caelo	Midazolam hydrochloride	15224611	30	1917S-03538
Fagron	Midazolam hydrochloride	15J07-B01-320717	40	1917Q-03538
Fagron	Midazolam hydrochloride	18B28-B05-354856	40	1919J-03538
Fagron	Midazolam hydrochloride	15J07-B01-320717	30	1917Q-03538
Fagron	Midazolam hydrochloride	15H04-B03-314396	30	1917R-03538
Fagron	Midazolam hydrochloride	18B28-B05-354856	40	1919J-03538
Caelo	Mistletoe, cut	11294003	30	20111027
Caelo	Morphine hydrochloride	15439411	40	1917R-01879
Caelo	Morphine hydrochloride	18188607	40	1919Q-01879
Caelo	Morphine hydrochloride	16184605	40	1917S-01879
Caelo	Morphine hydrochloride	15439411	40	1917R-01879
Caelo	Morphine hydrochloride	18188607	40	1919Q-01879
Fagron	Morphine hydrochloride	16D21-B02-322088	40	1917Q-01879
Fagron	Morphine hydrochloride	17F22-B01-338170	40	1919I-01879

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continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Fagron	Morphine hydrochloride	16D21-B02-322088	40	1917Q-01879
Fagron	Morphine hydrochloride	17F22-B01-338170	40	1919I-01879
Caelo	Morphine sulfate	15295802	40	1917R-07776
Caelo	Morphine sulfate	17331510	40	2319I-07776
Caelo	Morphine sulfate	12153212	60	0914F-07776
Caelo	Morphine sulfate	11333103	29	0914E-07776
Caelo	Morphine sulfate	15255703	60	1416Q-07776
Caelo	Morphine sulfate	15295802	40	1917R-07776
Caelo	Morphine sulfate	17331510	40	2319I-07776
Fagron	Morphine sulfate	14F02-B06-315405	40	1917Q-07776
Klenk	Motherwort herb, cut	4071A121211	40	20130104
Caelo	Mullein flower	11366403	40	20120105
Caelo	Mullein flower, cut	11233402	60	20110914
Caelo	Myrrh	11277111	60	1403081
Caelo	Myrrh	12269901	40	1403470
Klenk	Myrrh	3355B120628	40	AR-15-FG-000945-01
Caelo	Nettle leaf, cut	12184702	40	20120628
Galke	Nettle leaf, cut	21238	40	from supplier
Caelo	Nettle root, cut	11254903	40	20111121
Caelo	Nettle seed	12131507	40	1402203
Caelo	Nettle seed	11126211	40	pending
Caelo	Nettle seed	13387110	40	1410300
Klenk	Nettle seed	7470A111117	40	pending
Fagron	Nifedipine	18K19-B02-363428	40	20190122
Fagron	Nitrofurantoin	12C30-N03	40	1401461
Fagron	Nitrofurantoin	11K-21-N23	40	20111128
Fagron	Nitrofurantoin	12C30-N03	40	20120417
Fagron	Nitrofurantoin	13B28-N07	40	20130304
Fagron	Nitrofurantoin	11I07-N11	40	20110829
Fagron	Nitrofurantoin	15J15-B06-315225	60	AR-16-FG-003763-01
Fagron	Nitrofurantoin	15J15-B06-315225	60	20151028
Caelo	Nutmeg	12067304	40	20120320
Caelo	Nutmeg	13266002	40	20130906
Klenk	Nutmeg	7320A121002	40	20121012
Klenk	Nutmeg, powdered (spice)	7325A160405	60	9888
Caelo	Oak bark, cut	10348617	40	20101221
Caelo	Oak bark, cut	11351207	40	1403492
Caelo	Oak bark, cut	13360306	40	20131203
Caelo	Oak bark, powdered	11235004	40	20110909
Caelo	Oat straw, cut	11280008	40	20111020
Caelo	Olive leaf	11270106	40	20111013
Caelo	Olive leaf	12316808	60	AR-15-FG-001051-01
Caelo	Orris root	12206802	40	20120813
Caelo	Oxycodone hydrochloride	15220205	40	2017A-07734
Caelo	Oxycodone hydrochloride	17270202	40	1919Q-07734
Caelo	Oxycodone hydrochloride	15220205	40	2017A-07734
Caelo	Oxycodone hydrochloride	17270202	40	1919Q-07734
AppliChem	Papain	1G000215	40	1407433
Klenk	Parsley herb, rubbed	4262A091116	60	20110719
Caelo	Parsley root, cut	12080301	40	20120329
Klenk	Parsley seed	7370A130909	40	1407600
Klenk	Passionflower herb, cut	4231A120329	40	20120419
Klenk	Peony root, cut	6421B120327	60	20120403
Caelo	Peppermint leaf, cut	11347607	40	20111220
Caelo	Peppermint leaf, cut	11294401	40	20111104
Caelo	Peppermint leaf, cut	12321503	130	20121026
Caelo	Peppermint leaf, cut	13288303	40	20131002
Galke	Peppermint leaf, cut	20244	40	20120518
Galke	Peppermint leaf, cut	19537	40	from supplier
Fagron	Phenobarbital	16G20-B04-328344	40	2017B-01040

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Fagron	Phenobarbital	16G20-B04-328344	40	2017B-01040
Th. Geyer	Phenobarbital	067056	40	2017A-01040
Caelo	Pine sprouts, cut	11164708	60	20110610
Caelo	Pine sprouts, cut	13256105	40	20130828
Caelo	Piper cubeba	11081903	40	20110404
Caelo	Podophyllum resin (from podophyllum peltatum)	12287810	40	1405242
Caelo	Potassium bromide	11208211	40	20110803
Caelo	Potassium carbonate	180995	40	20180412*
Euro OTC	Potassium hydrocarbonate	1805027-01	40	20180606
Caelo	Potassium hydrogen phosphate	172493	40	20170911*
Caelo	Potassium hydroxide	180083	40	20180118*
Caelo	Potassium iodide	11090222	40	20110415
Caelo	Potassium metabisulfite	12325906	40	20121106
Caelo	Potassium monohydrogen phosphate	12366501	40	10401307
Caelo	Potassium nitrate	12236703	40	20120807
Euro OTC	Potassium orotate	1203038V-02	40	from supplier
Flora Apothek. ...	Potassium orotate	ORK00119	40	from supplier
Flora Apothek. ...	Potassium orotate	ORK00117	40	from supplier
Euro OTC	Potassium permanganate	1708016-02	40	20170824
Fagron	Prednisolone 1:10 (rice starch)	16F09-B04-341023	40	20161012
Sigma-Aldrich	Prednisolone pivalate	P2805000	40	CRS
Caelo	Primrose flower	11206806	100	20110809
Caelo	Primrose flower	11268002	40	20111007
Caelo	Primrose root, cut	12064506	40	20120319
Caelo	Propolis extract (96%) 2:1	11124120	40	1403460
Caelo	Propolis extract (96%) 2:1	13396103	40	20131212
Caelo	Propolis extract (96%) 2:1	13396103	40	20131212
Caelo	Psyllium seed	10291206	40	pending
Caelo	Psyllium seed	10291205	80	20101119
Caelo	Psyllium seed	13305903	40	pending
Caelo	Pumpkin seed, peeled	12249002	40	1404542
Caelo	Pumpkin seed, peeled	12249006	40	20120917
Dr. Behr	Quercetin	WE-13030084-02	40	from supplier
Caelo	Ramsons herb, cut	12380801	40	1404538
Caelo	Ramsons herb, cut	13072801	40	20130326
Caelo	Raspberry leaf, cut	12362701	40	20121219
Caelo	Red poppy petals, cut	12008104	40	20120131
Caelo	Red-rose petal	11299204	40	from supplier
Caelo	Red-rose petal, cut	11304912	40	20111107
Caelo	Redwood	12049604	40	20120229
Caelo	Restharrow root, cut	12330001	40	20121127
Klenk	Restharrow root, cut	6411B130404	40	20130507
Caelo	Rhubarb, cut	11057818	40	20110314
Caelo	Rhubarb, cut	12211906	40	20120827
Caelo	Rhubarb, cut	13235213	40	20130822
Caelo	Rhubarb, powdered	11043818	60	1403280
Caelo	Rhubarb, powdered	16009901	60	9886
Caelo	Ribwort plantain, cut	12362902	40	20121220
Caelo	Rifampicin	152446	40	20150831*
Caelo	Rifaximin	161053	60	20160607*
Caelo	Rose hips peel, cut	11301407	60	20111110
Klenk	Rose hips seed	7240A120402	60	20120404
Caelo	Rose hips with peel, cut	12064202	40	20120328
Caelo	Rose hips with peel, cut	11232204	40	20110919
Caelo	Rose mallow flower, cut	10244508	60	20100917
Caelo	Roselle	12007311	60	20120124

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Roselle	11036509	60	20110303
Caelo	Rosemary leaf, cut	11193408	40	20110728
Caelo	Rosemary leaf, cut	14159601	60	20140617
Klenk	Rosemary leaf, cut	2261A131118	60	AR-15-FG-008499-01
Klenk	Ruscus rhizome, cut	7081B110301	60	20130131
Fagron	Rutoside trihydrate	13K12-B06-295483	60	20131204
Klenk	Saffron (spice)	0384A121022	40	20121114
Caelo	Sage leaf, cut	11347503	40	20120102
Fagron	Salbutamol sulfate	13K12-N02	60	20131114
Fagron	Salbutamol sulfate	13K12-N02	40	20131114
Fagron	Salbutamol sulfate	13K12-N02	40	1801521
Fagron	Salbutamol sulfate	13K12-N02	40	20131107
Fagron	Salbutamol sulfate	13K12-N02	40	20131107
Fagron	Salbutamol sulfate	13K12-N02	40	20131114
Fagron	Salbutamol sulfate	13K12-N02	40	20131114
Fagron	Salbutamol sulfate	17I21-B02	40	20170311
Caelo	Sarsaparilla root, cut	10230402	60	20100909
Euro OTC	Selenium disulfide	1411011-02	40	20141211
Caelo	Senna leaf, cut	12273106	40	20120927
Caelo	Senna leaf, powdered	11193307	120	pending
Caelo	Senna leaf, powdered	12369908	40	1408079
Klenk	Senna leaf, powdered	2334B130606	60	AR-15-FG-015212-01
Caelo	Senna pods, tinnevelly	12267605	40	20120921
Caelo	Senna pods, tinnevelly	11154404	40	20110607
Caelo	Senna pods, tinnevelly	13395106	40	20140106
EDQM	Sertaconazole nitrate	2.0	26	CRS
Caelo	Shepherd's purse, cut	11328208	40	20111205
Caelo	Siam benzoin	12321314	40	20121031
Caelo	Silica, colloidal anhydrous	181124	40	20180424*
Caelo	Silver nitrate	181276	40	20180716*
Caelo	Silver, colloidal, for external use	173615	40	20180312*
Caelo	Silverweed, cut	11328105	40	20111130
Galke	Silverweed, cut	22840	40	from supplier
Fagron	Sodium alginate	14G22-B99-297091	60	20140813
Caelo	Sodium bromide	171191	40	20170510*
Caelo	Sodium carbonate decahydrate	173613	40	20180115*
Caelo	Sodium carbonate monohydrate	16310205	40	20161221
Yino Pharma	Sodium chondroitin sulfate	YN010511806007	40	20180912*
Yino Pharma	Sodium chondroitin sulfate	YN010511805005	40	20180912*
Pharmorgana	Sodium dichloroacetate	1000150016	40	from supplier
Caelo	Sodium dihydrogen phosphate dihydrate	12198506	40	20120705
Euro OTC	Sodium dihydrogen phosphate dihydrate	1202015-01	40	20120221
Euro OTC	Sodium hydrocarbonate	1807021-01	40	20180725
Fagron	Sodium hydroxide pellets	12E02-N15	80	20120521
Caelo	Sodium iodide	161701	40	20160706*
Euro OTC	Sodium molybdate dihydrate	L1305049-01	45	20130806
Euro OTC	Sodium molybdate dihydrate	L1305049-01	60	20130806
Caelo	Sodium monohydrogenphosphate heptahydrate	12109002	40	20120424
Caelo	Sodium nitrate	11045910	40	20110225
Caelo	Sodium nitrite	171360	30	20170522*
Caelo	Sodium perborate, hydrated	11158903	40	20110616
Euro OTC	Sodium sulfate decahydrate	1708012-02	40	20171005

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Euro OTC	Sodium sulfate, anhydrous	1801046-01	40	20180202
Caelo	Sodium thiosulfate pentahydrate	181648	40	20180712*
Caelo	Solanum dulcamara stems, cut	10375602	40	20110113
Caelo	Solanum dulcamara stems, cut	13254305	40	20130806
Inresa	Sotalol hydrochloride	369-MC	40	20150527
Caelo	Sour cherry stems, cut	12042302	40	1503570
Caelo	Spearmint leaf, cut	12133906	40	20120516
Caelo	Star anise	11314104	10	20111121
Caelo	Star anise, cut	12226301	60	pending
Caelo	Star anise, cut	13041401	40	1403709
Caelo	Star anise, cut	15329302	60	AR-16-FG-004770-01
Caelo	Stemless carline root	12163702	40	20120628
Caelo	Strawberry leaf, cut	11117903	40	20110428
Klenk	Strawberry leaf, cut	2031B110224	40	20110304
Klenk	Strawberry leaf, cut	2031B120925	40	20121005
Caelo	Sulfamerazine	10218403	30	20100914
Fagron	Sunset yellow	13I05_N04	40	20130903
Klenk	Sweet fennel	2870A110412	40	pending
Klenk	Sweet fennel	2870A130304	40	1405154
Caelo	Sweet woodruff herb, cut	10375812	30	20110114
Euro OTC	Tacrolimus monohydrate	1904015	40	20190617*
Euro OTC	Tacrolimus monohydrate	1904015	40	20190617*
Caelo	Talcum	11318312	80	1405338
Otto Fischar	Talcum	90841/1	40	from supplier
Roth	Theobromine, 99%	145191010	60	AR-16-FG-002141-01
Roth	Theobromine, 99%	365191010	60	20120829
Fagron	Theophylline-ethylenediamine	19C04-B04-363517	40	20190823
Caelo	Theriac, powdered	12289307	40	1405122
Caelo	Theriac, powdered	13407301	40	1410336
Klenk	Theriac, powdered	13816	60	1705088
Fagron	Thiamine nitrate	15A30-B06-309069	60	AR-16-FG-005855-01
Caelo	Thiomersal	172173	30	20170919*
Fagron	Thiomersal	11K01-N03	40	1401417
Caelo	Thyme, rubbed	11345004	60	20111213
Galke	Thyme, rubbed	21932	40	from supplier
Euro OTC	Titanium dioxide	1708015-01	40	20170822
Carotech	Tocomax 15%	100912	40	from supplier
Caelo	Tonka beans	12145101	40	20120604
Caelo	Tormentil	12040708	40	1403487
Caelo	Tormentil	12013103	40	1403048
Caelo	Tormentil	12040715	40	1403710
Caelo	Tormentil	13220502	40	1403049
Caelo	Tormentil	14360103	60	1606520
Klenk	Tormentil	6914B120112	40	20120118
Caelo	Tragacanth, powdered	13277804	60	1507149
Caelo	Tragacanth, powdered	15085602	60	20150410
Caelo	Tragacanth, powdered	15379906	60	20151124
Caelo	Tragacanth, powdered	16110802	60	AR-17-FG-007533-01
Caelo	Tribromophenol bismuth	18144202	40	20180706
Euro OTC	Tricalcium phosphate	1206002-01	40	1402298
Roth	Trypan blue (C.I. 23850)	204209355	60	from supplier
Caelo	Turmeric root, cut	11160403	60	20110628
Caelo	Turmeric root, cut	12136503	40	1405295
Caelo	Turmeric root, cut	13360202	40	1411363
Caelo	Turmeric, javanese, cut	12185605	40	1403465
Caelo	Turmeric, javanese, cut	12319206	40	20121130

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra	Certificate
Caelo	Turmeric, javanese, cut	13262904	40	20130926
Kräuter Schulte	Twotoothed achyranthes root, cut	45053	40	from supplier
Caelo	Valerian root, cut	12033809	40	20120228
Caelo	Valerian root, powdered	12138005	40	1403809
Caelo	Valerian root, powdered	12138008	40	1508496
Caelo	Valerian root, powdered	13113204	60	pending
Caelo	Verbena herb, cut	12187602	40	20120719
Klenk	Verbena herb, cut	4651B120611	40	20121123
Caelo	Walnut bark, cut	11325603	40	20111124
Caelo	Walnut leaf, cut	11103007	40	1403091
Caelo	White deadnettle flower	11371604	40	20120103
Caelo	White mustard seed	12361002	40	1403473
Caelo	White mustard seed	13064301	40	pending
Caelo	White mustard seed	13380501	40	20140103
Caelo	White mustard seed, powdered	12349601	60	1403281
Caelo	White mustard seed, powdered	12375705	40	20130110
Caelo	White pepper	12294902	40	1403488
Caelo	White pepper	12294905	40	20121130
Caelo	White pepper	14010703	40	20140122
Caelo	Wild pansy, cut	10291007	60	20101103
Caelo	Willow bark, cut	12185204	40	20120730
Caelo	Willow herb, cut	11347311	40	20111216
Caelo	Willowherb, small flowered, cut	10326106	40	20101216
Caelo	Willowherb, small flowered, cut	13355904	60	20140113
Klenk	Willowherb, small flowered, cut	4721A140203	60	20140219
Caelo	Wormwood herb, cut	12355801	40	20121211
Dr. Behr	Yam root extract	WE14020005-05	40	pending
Caelo	Yarrow flower, rubbed	12267703	40	20120921
Caelo	Yellow chaste weed, cut	11293101	40	20111028
Caelo	Zedoary root, cut	12125301	40	20120522
Caelo	Zedoary root, powdered	12344601	40	1403489
Caelo	Zedoary root, powdered	13165501	40	pending
Caelo	Zedoary root, powdered	14249001	60	20141008
Caelo	Zinc chloride	11345504	40	20111222
Euro OTC	Zinc orotate dihydrate	1203014-01	40	20120705
Euro OTC	Zinc orotate dihydrate	1203014-01	40	1407431
Euro OTC	Zinc orotate dihydrate	13050005-02	40	20130628
Fagron	Zinc orotate dihydrate	13J08-N05	40	20130212
Caelo	Zinc oxide	14038101	40	20140205
Caelo	Zinc oxide-talcum powder mixture 1:1	181487	40	20180702*
Caelo	Zinc stearate	182279	40	20181017*
Caelo	Zinc sulfate heptahydrate	12257802	40	20120830

*The spectra were taken from a part of the same sample which the supplier used for its analysis (identity, purity, content). In this case the manufacturer certificates proof the identity and quality of the sample from those the spectra descend.

Appendix C: Additional validation samples (*Type C*)

Spectra for substances from the field which cannot be identified with this model also enter the validation. In this manner, it is verified that the model also rejects unknown substances. The spectra for these samples were recorded by *Apo-Ident* customers. They belong to *Type C*. The information provided by the customer regarding the manufacturer and batch number is taken over by *HiperScan GmbH* to a large extent unchecked.

The samples originate from 7724 batches. From these, 17 883 spectra were recorded. The spectra recorded on independent samples of substances from the field which can be identified with the model are listed respectively in the section *Type C* for the individual substances and do not appear again elsewhere in this list.

Supplier	Substance	Batch	Spectra
Fagron	(R,S)-epinephrine hyd...	14A22-B05	1
Fagron	(R,S)-epinephrine hyd...	2021503	1
Fagron	(R,S)-epinephrine hyd...	10022015E	1
Fagron	(R,S)-epinephrine hyd...	16H23-B98-325052	1
Dermapharm	8-quinolinol sulfate ...	140804	1
Dermapharm	8-quinolinol sulfate ...	100804	1
Fagron	8-quinolinol sulfate ...	10F01-N15	1
Fagron	8-quinolinol sulfate ...	11L08-N07	2
Fagron	8-quinolinol sulfate ...	11/09-N09	1
Fagron	8-quinolinol sulfate ...	11L19-N14	1
Fagron	8-quinolinol sulfate ...	13/21-N23	1
Fagron	8-quinolinol sulfate ...	13D24-N11	1
Fagron	8-quinolinol sulfate ...	13G10-N06	1
Fagron	8-quinolinol sulfate ...	12A04-N05	1
Fagron	8-quinolinol sulfate ...	11I09-N09	1
Fagron	8-quinolinol sulfate ...	13A04-N05	1
Fagron	8-quinolinol sulfate ...	12D26-N04	1
Fagron	8-quinolinol sulfate ...	12H21-N08	1
Fagron	8-quinolinol sulfate ...	13032014C	1
Dermapharm	8-quinolinol sulfate ...	120905	1
siehe WE-Prüfprotokoll	8-quinolinol sulfate ...	96/09	1
Caelo	Abrotani herb, cut	2091305	1
Klenk	Abrotani herb, cut	21081301	1
Klenk	Abrotani herb, cut	26011403	1
Nachprüfung	Abrotani herb, cut	3451A070919	1
Noweda	Abrotani herb, cut	3451A120312	19
Bombastus	Acorus root, natural,...	276260	2
Bombastus	Acorus root, natural,...	224114	1
Bombastus	Acorus root, natural,...	281692	2
Bombastus	Acorus root, natural,...	277958	1
Bombastus	Acorus root, natural,...	274159	1
Caelo	Acorus root, natural,...	13127801	1
Caelo	Acorus root, natural,...	284875	2
Klenk	Acorus root, natural,...	B130807	1
Caelo	Acorus root, natural,...	12066501	1
Aurica/Phönix	Acorus root, peeled	150649	1
Bahnhof-Apotheke	Acorus root, peeled	17-121107	1
Bombastus	Acorus root, peeled	267365	1
Bombastus	Acorus root, peeled	274159	3
Caelo	Acorus root, peeled	15061202	1
Caelo	Acorus root, peeled	24081203	1
Caelo	Acorus root, peeled	12056703	1
Caelo	Acorus root, peeled	12066501	7
Caelo	Acorus root, peeled	12066502	1
Caelo	Acorus root, peeled	28121205	1
Caelo	Acorus root, peeled	8031306	1
Caelo	Acorus root, peeled	12295901	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Acorus root, peeled	6701B130103	21
Caelo	Acorus root, peeled	12295904	4
Caelo	Acorus root, peeled	7061302	1
Caelo	Acorus root, peeled	313060	1
Caelo	Acorus root, peeled	12295903	1
Caelo	Acorus root, peeled	12275602	7
Caelo	Acorus root, peeled	241013010	1
Caelo	Acorus root, peeled	12275604	2
Caelo	Acorus root, peeled	12056701	1
Caelo	Acorus root, peeled	12295902	4
Caelo	Acorus root, peeled	12239008	1
Caelo	Acorus root, peeled	12275604-3544411013	1
Caelo	Acorus root, peeled	13101306	1
Galke	Acorus root, peeled	18944	1
Gehe	Acorus root, peeled	6701B130807	9
Klenk	Acorus root, peeled	6701B150407	1
Klenk	Acorus root, peeled	106212173	1
Klenk	Acorus root, peeled	6701B120427	7
Klenk	Acorus root, peeled	6701B120817	6
Klenk	Acorus root, peeled	6701B130870	1
Klenk	Acorus root, peeled	6711B110606	1
Klenk	Acorus root, peeled	4797362	1
Klenk	Acorus root, peeled	6701b120301	1
Klenk	Acorus root, peeled	6701b130103	1
Klenk	Acorus root, peeled	6701B120301	3
Caelo	Agarikon	11024502	1
Berkel AHK	Agnus castus fruit	14194401	4
Caelo	Agnus castus fruit	11026309	1
Caelo	Agnus castus fruit	12016909	4
Caelo	Agnus castus fruit	12016902	1
Caelo	Agnus castus fruit	12016908	1
Caelo	Agnus castus fruit	12274010	10
Caelo	Agnus castus fruit	12274008	1
Caelo	Agnus castus fruit	12274009	3
Caelo	Agnus castus fruit	12274014	1
Caelo	Agnus castus fruit	13193401	2
Caelo	Agnus castus fruit	13193403	1
Caelo	Agnus castus fruit	1513546	1
Caelo	Agnus castus fruit	13193407	1
Caelo	Agnus castus fruit	13193410	2
Caelo	Agnus castus fruit	14194408	1
Caelo	Agnus castus fruit	15318702	1
Caelo	Agnus castus fruit	15318705	1
Caelo	Agnus castus fruit	15318718	1
Caelo	Agnus castus fruit	12274002	1
Caelo	Agnus castus fruit	13193406	1
Caelo	Agnus castus fruit	15065105	1
Caelo	Agnus castus fruit	11026318	1
Caelo	Agnus castus fruit	12274013	2
Caelo	Agnus castus fruit	3413A-03015	1
Caelo	Agnus castus fruit	80175158	2
Caelo	Agnus castus fruit	12016905	2
Caelo	Agnus castus fruit	13193404	1
Gutenberg-Apotheke	Agnus castus fruit	61765	1
Klenk	Agnus castus fruit	A120803	1
Klenk	Agnus castus fruit	7110N090701	1
Klenk	Agnus castus fruit	A110614	3
Klenk	Agnus castus fruit	7110A120803	1
Klenk	Agnus castus fruit	7110A110614	2
Klenk	Agnus castus fruit	A130613	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Agnus castus fruit	7110N150121	1
Klenk	Agnus castus fruit	7110A130613	1
Klenk	Agnus castus fruit	12274007	3
Sanacorp	Agnus castus fruit	12274006	3
Caelo	Agnus castus fruit	12274003	4
Caelo	Agnus castus fruit	12274012	1
Alliance	Agrimony, cut	11374004	5
Anzag 05.12.12	Agrimony, cut	11374002	3
Caelo	Agrimony, cut	10325502	2
Caelo	Agrimony, cut	10325505	1
Caelo	Agrimony, cut	12382903	1
Caelo	Agrimony, cut	1137407	1
Caelo	Agrimony, cut	11374005	2
Caelo	Agrimony, cut	12382901	3
Caelo	Agrimony, cut	3481-A-110324	1
Caelo	Agrimony, cut	11374006	6
Celo	Agrimony, cut	11374003	1
Galke	Agrimony, cut	2002	1
Herbasinica	Agrimony, cut	11374007	1
Klenk	Agrimony, cut	3481C120508	1
Noweda	Agrimony, cut	9300106	1
Noweda	Agrimony, cut	10325503	2
Sino Phyto	Agrimony, cut	12382905	5
Caelo	Alchemilla alpina her...	12147202	3
Caelo	Alchemilla alpina her...	12147205	2
Caelo	Alchemilla alpina her...	12147203	1
Caelo	Alchemilla alpina her...	1214204	1
Caelo	Alchemilla alpina her...	12147203-3470312131	1
Caelo	Alchemilla alpina her...	11063608	1
Caelo	Alchemilla alpina her...	12147206	3
Alfred Galke	Alchemilla, cut	20921	1
Caelo	Alchemilla, cut	13141105	3
Anzag ek: 6,39 11,09...	Alchemilla, cut	11182806	6
Bombastus	Alchemilla, cut	279070	5
Bahnhof-Apotheke	Alchemilla, cut	17-121107	1
Bombastus	Alchemilla, cut	272021	5
Bombastus	Alchemilla, cut	276173	3
Bombastus	Alchemilla, cut	278889	1
Bombastus	Alchemilla, cut	282032	2
Bombastus	Alchemilla, cut	14066007	1
Bombastus	Alchemilla, cut	521203995	1
Bombastus	Alchemilla, cut	266404	1
Bombastus	Alchemilla, cut	231013B	1
Caelo	Alchemilla, cut	1100912	1
Caelo	Alchemilla, cut	11002906	5
Caelo	Alchemilla, cut	11182801	3
Caelo	Alchemilla, cut	11182804	3
Caelo	Alchemilla, cut	1406211616	1
Caelo	Alchemilla, cut	11182807	2
Caelo	Alchemilla, cut	21081203	1
Caelo	Alchemilla, cut	11182805	1
Caelo	Alchemilla, cut	11063605	1
Caelo	Alchemilla, cut	11182808	1
Caelo	Alchemilla, cut	12153301	3
Caelo	Alchemilla, cut	8121201	1
Caelo	Alchemilla, cut	12153303	7
Caelo	Alchemilla, cut	12153305	25
Caelo	Alchemilla, cut	12153307	3
Caelo	Alchemilla, cut	12342901	1
Caelo	Alchemilla, cut	5041301	1

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Supplier	Substance	Batch	Spectra
Caelo	Alchemilla, cut	125306	1
Caelo	Alchemilla, cut	H-040513-2	1
Caelo	Alchemilla, cut	13141103	36
Caelo	Alchemilla, cut	2081304	1
Caelo	Alchemilla, cut	intch:318080	1
Caelo	Alchemilla, cut	3613M01616	1
Caelo	Alchemilla, cut	13091304	1
Caelo	Alchemilla, cut	13141106	8
Caelo	Alchemilla, cut	9011405	1
Caelo	Alchemilla, cut	27011401	1
Caelo	Alchemilla, cut	14066002	2
Caelo	Alchemilla, cut	14066008	1
Caelo	Alchemilla, cut	15147002	2
Caelo	Alchemilla, cut	1118206	1
Caelo	Alchemilla, cut	1213309	1
Caelo	Alchemilla, cut	1215305	2
Caelo	Alchemilla, cut	131411002	1
Caelo	Alchemilla, cut	13141102	6
Caelo	Alchemilla, cut	5013I1616	1
Caelo	Alchemilla, cut	13141101	7
Caelo	Alchemilla, cut	1215309	1
Caelo	Alchemilla, cut	13141103-3382319003	1
Caelo	Alchemilla, cut	13141103-3400310161	1
Caelo	Alchemilla, cut	13141103-3456311103	1
Caelo	Alchemilla, cut	13141106-3545412081	1
Galke	Alchemilla, cut	21141	1
Galke	Alchemilla, cut	22291	1
Galke	Alchemilla, cut	19835	1
Gehe	Alchemilla, cut	1341102	1
Klenk	Alchemilla, cut	3501C121105	4
Hepart AG	Alchemilla, cut	21963	3
Hepart AG	Alchemilla, cut	B-698kbA	1
Ichtyol/Phönix	Alchemilla, cut	13141107	3
Klenk	Alchemilla, cut	3501B100428	1
Klenk	Alchemilla, cut	3501B090417	1
Klenk	Alchemilla, cut	3501A110301	3
Noweda	Alchemilla, cut	12153302	13
Caelo	Alchemilla, cut	14066003	1
Sanacorp	Alchemilla, cut	12153309	14
Caelo	Alchemilla, cut	12153306	5
Fagron	Alchemilla, cut	11182802	1
Wolf	Alchemilla, cut	E-822	1
Wolf	Alchemilla, cut	B-698	2
Wolf	Alchemilla, cut	23187	4
Wolf	Alchemilla, cut	p931	1
Klenk	Almonds, bitter, whole	40A161028	13
Klenk	Almonds, bitter, whole	40A-150904	2
Klenk	Almonds, bitter, whole	40A161206	8
Apotheke Bühlau	Almonds, bitter, whole	267467	2
Bombastus	Almonds, bitter, whole	275001	3
Bombastus	Almonds, bitter, whole	275600	1
Bombastus	Almonds, bitter, whole	283369	1
Bombastus	Almonds, bitter, whole	284978	1
Bombastus	Almonds, bitter, whole	297921	1
Bombastus	Almonds, bitter, whole	304961	1
Bombastus	Almonds, bitter, whole	1700352	2
Bombastus	Almonds, bitter, whole	17000353	1
Bombastus	Almonds, bitter, whole	306048	1
Bombastus	Almonds, bitter, whole	303218	2
Bombastus	Almonds, bitter, whole	305322	2

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Supplier	Substance	Batch	Spectra
Bombastus	Almonds, bitter, whole	275601	1
Bombastus	Almonds, bitter, whole	267529	1
Caelo	Almonds, bitter, whole	12239604	1
Caelo	Almonds, bitter, whole	13242001	1
Caelo	Almonds, bitter, whole	5121301	1
Caelo	Almonds, bitter, whole	15193103	1
Euro OTC	Almonds, bitter, whole	290973	2
Fagron	Almonds, bitter, whole	40A161005	4
Caelo	Almonds, bitter, whole	16221202	1
Klenk	Almonds, bitter, whole	40A150904	12
Klenk	Almonds, bitter, whole	40A120924	4
Klenk	Almonds, bitter, whole	40A121010	11
Klenk	Almonds, bitter, whole	40A111004	1
Klenk	Almonds, bitter, whole	40A111117	7
Klenk	Almonds, bitter, whole	40A140908	19
Klenk	Almonds, bitter, whole	40A0130909	1
Klenk	Almonds, bitter, whole	40A130909	9
Klenk	Almonds, bitter, whole	40A150905	1
Klenk	Almonds, bitter, whole	40A0161005	1
Caelo	Aloes, cape, cut	12232102	1
Caelo	Aloes, cape, cut	505125	1
Caelo	Aloes, cape, cut	12338206	2
Caelo	Aloes, cape, cut	25111303	1
Caelo	Aloes, cape, cut	12338209	1
Caelo	Aloes, cape, cut	11041402	1
Caelo	Aloes, cape, cut	11061406	1
Caelo	Aloes, cape, cut	25071402	1
Caelo	Aloes, cape, cut	16202404	2
Caelo	Aloes, cape, cut	16202407	1
Caelo	Aloes, cape, cut	16202403	1
Caelo	Aloes, cape, cut	15283001	1
Caelo	Aloes, cape, cut	12338201	4
Caelo	Aloes, cape, cut	15283010	2
Caelo	Aloes, cape, cut	16202401	2
Caelo	Aloes, cape, cut	12338203	4
Caesar/Noweda	Aloes, cape, cut	2013E-01089	1
Caesar/Noweda	Aloes, cape, cut	12338211	1
phönix	Aloes, cape, cut	15283011	2
Caelo	Aloes, cape, cut	15283007	1
Caelo	Aloes, cape, cut	16202406	2
Anzag 22.03.13 ek: 5,...	Aloes, cape, powdered	12232102	1
Caelo	Aloes, cape, powdered	11132115	1
Caelo	Aloes, cape, powdered	12183007	1
Caelo	Aloes, cape, powdered	12183009	3
Caelo	Aloes, cape, powdered	14065905	1
Caelo	Aloes, cape, powdered	15206501	1
Caelo	Aloes, cape, powdered	12183008	1
Caelo	Aloes, cape, powdered	12183001	1
Caelo	Aloes, cape, powdered	14065906	1
Caelo	Aloes, cape, powdered	11132116	2
Caelo	Aloes, cape, powdered	15206514	1
Caelo	Aloes, cape, powdered	15206516	1
Caelo	Aloes, cape, powdered	15206507	1
Caelo	Aloes, cape, powdered	11132116	1
Caelo	Aloes, cape, powdered	12183013	3
Caelo	Aloes, cape, powdered	16202410	1
Anzag	Aluminium chloride he. ...	1204026-02	16
Fagron	Aluminium chloride he. ...	12127-N01	4
Caelo	Aluminium chloride he. ...	11229917	3
Caelo	Aluminium chloride he. ...	11229905	1

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Supplier	Substance	Batch	Spectra
Caelo	Aluminium chloride he...	11229907	1
Caelo	Aluminium chloride he...	3091205	1
Caelo	Aluminium chloride he...	12114906	6
Caelo	Aluminium chloride he...	12114904	2
Caelo	Aluminium chloride he...	23111203	1
Caelo	Aluminium chloride he...	11229906	1
Caelo	Aluminium chloride he...	10251307	1
Caelo	Aluminium chloride he...	12021303	1
Caelo	Aluminium chloride he...	8031301	1
Caelo	Aluminium chloride he...	12114918	18
Caelo	Aluminium chloride he...	12114920	11
Caelo	Aluminium chloride he...	19041302	1
Caelo	Aluminium chloride he...	10251314	1
Caelo	Aluminium chloride he...	15051302	1
Caelo	Aluminium chloride he...	12114919	1
Caelo	Aluminium chloride he...	18061308	1
Caelo	Aluminium chloride he...	9071303	1
Caelo	Aluminium chloride he...	12323711	17
Caelo	Aluminium chloride he...	5081301	1
Caelo	Aluminium chloride he...	12323710	8
Caelo	Aluminium chloride he...	28121301	1
Caelo	Aluminium chloride he...	12323717	5
Caelo	Aluminium chloride he...	15080701	1
Caelo	Aluminium chloride he...	13L13-B03-287298	1
Caelo	Aluminium chloride he...	15080715	1
Caelo	Aluminium chloride he...	11229914	1
Caelo	Aluminium chloride he...	12114908	8
Caelo	Aluminium chloride he...	12114922	14
Caelo	Aluminium chloride he...	13G03-N02	21
Caelo	Aluminium chloride he...	12127-N01	1
Caelo	Aluminium chloride he...	3113E-01095	1
Caelo	Aluminium chloride he...	12114912	4
Caelo	Aluminium chloride he...	13/13-B03-287298	1
Caesar & Loretz GmbH,...	Aluminium chloride he...	12047508	4
Caesar & Loretz GmbH,...	Aluminium chloride he...	12323702	14
EuRho	Aluminium chloride he...	1106017-01	1
EuRho	Aluminium chloride he...	2512I01095	1
EuRho	Aluminium chloride he...	d024a	1
Euro OTC	Aluminium chloride he...	120402601	3
EuRho Pharm	Aluminium chloride he...	1109025-02	3
Euro OTC	Aluminium chloride he...	1213M-01095	1
Euro OTC	Aluminium chloride he...	1210014-01	25
Euro OTC	Aluminium chloride he...	1307011-02	2
Euro OTC	Aluminium chloride he...	1204026-01	20
Euro OTC	Aluminium chloride he...	1103007-01	1
Euro OTC	Aluminium chloride he...	1109025-01	1
Euro OTC	Aluminium chloride he...	1507002-01	1
Euro OTC	Aluminium chloride he...	1307011-01	10
Euro OTC	Aluminium chloride he...	1307011	1
Euro OTC	Aluminium chloride he...	1210012-01	1
Euro OTC	Aluminium chloride he...	2111Q-01095	1
EUro/AHD	Aluminium chloride he...	121001401	3
Euroo/Phoenix	Aluminium chloride he...	120014-02	1
Euro OTC	Aluminium chloride he...	co31a	1
Euro OTC	Aluminium chloride he...	1210014-02	30
Euro OTC	Aluminium chloride he...	121001402	1
Fagron	Aluminium chloride he...	11G05-No2	1
Fagron	Aluminium chloride he...	1207211095	1
Fagron	Aluminium chloride he...	11123-N06	3
Fagron	Aluminium chloride he...	1910211095	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Aluminium chloride he...	C181A	2
Fagron	Aluminium chloride he...	12/27-N01	7
Fagron	Aluminium chloride he...	C012A	1
Fagron	Aluminium chloride he...	11 23-N06	1
Fagron	Aluminium chloride he...	11/23-N06	2
Fagron	Aluminium chloride he...	11G05-N02	1
Fagron	Aluminium chloride he...	105282-0001	1
Fagron	Aluminium chloride he...	11/23-N06B206A	1
Fagron	Aluminium chloride he...	8547287	1
Fagron	Aluminium chloride he...	2013U-01095	1
Fagron	Aluminium chloride he...	12i27-N01	2
Fagron	Aluminium chloride he...	13D22N09	2
Fagron	Aluminium chloride he...	13D22-N09	25
Fagron	Aluminium chloride he...	C145A	1
Fagron	Aluminium chloride he...	2913U1095	1
Fagron	Aluminium chloride he...	12082013D	1
Fagron	Aluminium chloride he...	20122013E	1
Fagron	Aluminium chloride he...	13I26-N13	2
Fagron	Aluminium chloride he...	13I26-N13	1
Fagron	Aluminium chloride he...	13J31-B06-287615	1
Fagron	Aluminium chloride he...	12C07-N01	7
Fagron	Aluminium chloride he...	12I27-N01	11
Fagron	Aluminium chloride he...	5213A1095	1
Fagron	Aluminium chloride he...	12G05-N10	23
Fagron	Aluminium chloride he...	12/27/N01	1
Fagron	Aluminium chloride he...	12L11-N03	3
Fagron	Aluminium chloride he...	12/27-n01	1
Fagron	Aluminium chloride he...	12/11-No3	1
Faron	Aluminium chloride he...	13I13-B03-287298	1
Gehe	Aluminium chloride he...	12114902	3
Gehe	Aluminium chloride he...	130701102	1
Caelo	Aluminium chloride he...	12114910	6
Euro OTC	Aluminium chloride he...	120402602	1
Euro OTC	Aluminium chloride he...	1406021-01	1
Euro OTC	Aluminium chloride he...	1210014-02-336331909	1
Fagron	Aluminium chloride he...	13d22no9	1
Caelo	Aluminium chloride he...	12047503	2
Caelo	Aluminium chloride he...	12047514	3
Caelo	Aluminium chloride he...		2
Caelo	Aluminium chloride he...	51/AD1	1
Fagron	Aluminium chloride he...	12047512	3
Caelo	Aluminium potassium s...	14263804	1
Alliance Health	Aluminium potassium s...	13025401	3
Alliance Healthcare	Aluminium potassium s...	13025404	1
Anzag	Aluminium potassium s...	1218441	1
Caelo	Aluminium potassium s...	1218411	1
Caelo	Aluminium potassium s...	12022444	1
Caelo	Aluminium potassium s...	12022404	1
Caelo	Aluminium potassium s...	510211092	1
Caelo	Aluminium potassium s...	11017211	1
Caelo	Aluminium potassium s...	12022406	2
Caelo	Aluminium potassium s...	12184401	2
Caelo	Aluminium potassium s...	12184407	3
Caelo	Aluminium potassium s...	504311092	1
Caelo	Aluminium potassium s...	90033229	1
Caelo	Aluminium potassium s...	12144605	4
Caelo	Aluminium potassium s...	12184408	3
Caelo	Aluminium potassium s...	12144607	2
Caelo	Aluminium potassium s...	12239102	2
Caelo	Aluminium potassium s...	13025401	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Aluminium potassium s...	12184411	1
Caelo	Aluminium potassium s...	2713Q1092	1
Caelo	Aluminium potassium s...	13025404	3
Caelo	Aluminium potassium s...	15172501	1
Caelo	Aluminium potassium s...	12184401	1
Caelo	Aluminium potassium s...	12144602	1
Caelo	Aluminium potassium s...	12184406	2
Caelo	Aluminium potassium s...	11254805	1
Caelo	Aluminium potassium s...	11218611	2
Caelo	Aluminium potassium s...	12184402	3
Caelo	Aluminium potassium s...	13098702	1
Caelo	Aluminium potassium s...	12184407	5
Caelo	Aluminium potassium s...	12022409	1
Caelo	Aluminium potassium s...	12022401	1
Caelo	Aluminium potassium s...	12022406	1
Caesar/Noweda	Aluminium potassium s...	12184411	2
Euro OTC	Aluminium potassium s...	1004046-02	1
Fagron	Aluminium potassium s...	A1-063-A1	1
Fagron	Aluminium potassium s...	12/24-M02	1
Fagron	Aluminium potassium s...	103638	1
Fagron	Aluminium potassium s...	A1-063-AL	1
Fagron	Aluminium potassium s...	13D08-N01	1
Caelo	Aluminium potassium s...	12 24-M03	1
Fagron	Aluminium potassium s...	13D29-N04	1
Sanacorp	Aluminium potassium s...	12184402	2
Caelo	Aluminium potassium s...	12144603	1
Fagron	Aluminium potassium s...	12I24-M03	1
Caesar/Noweda	American liverwort, cut	11254608	1
Ebert 04.04.2014	Amiloride hydrochloride	13J08-B04	1
Fagron	Amiloride hydrochloride	17J02-B04	1
Fagron	Amiloride hydrochloride	17J02-B04-341175	1
Caelo	Ammonium chloride	10176319	2
Caelo	Ammonium chloride	12240302	4
Caelo	Ammonium chloride	12356101	3
Caelo	Ammonium chloride	10176309	1
Euro OTC	Ammonium chloride	1212017-01	2
Euro OTC	Ammonium chloride	1303029-01	1
Euro OTC	Ammonium chloride	1203029-01	1
Euro OTC	Ammonium chloride	512A-01104	1
Caelo	Ammonium hydrogen car...	3091204	1
Caelo	Ammonium hydrogen car...	24101202	1
Caelo	Ammonium hydrogen car...	11145612	2
Caelo	Ammonium hydrogen car...	9139402	1
Caelo	Ammonium hydrogen car...	12022308	2
Caelo	Ammonium hydrogen car...	13104601	1
Caelo	Ammonium hydrogen car...	25111308	1
Caelo	Ammonium hydrogen car...	23011404	1
Caelo	Ammonium hydrogen car...	13104611	1
Caelo	Ammonium hydrogen car...	72715338	1
Caelo	Ammonium hydrogen car...	12322204	1
Caelo	Ammonium hydrogen car...	12322201	1
Caelo	Ammonium hydrogen car...	3712Q-01103	1
Caelo	Amphetamine sulfate	12I24-N03	1
Caelo	Amphetamine sulfate	13344609	1
Caelo	Amphetamine sulfate	15193204	1
Caelo	Amphetamine sulfate	16153903	4
Caelo	Amphetamine sulfate	16153909	1
Caelo	Amphetamine sulfate	1807171	1
Caelo	Amphetamine sulfate	17K03-B01	1
Caelo	Amphetamine sulfate	16143001	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Amphetamine sulfate	16153902	1
Caelo	Amphetamine sulfate	1ot067002	1
Caelo	Amphetamine sulfate	15L01-B05	3
Caelo	Amphetamine sulfate	16153905	2
Caelo	Amphetamine sulfate	12B06-N013	1
Fagron	Amphetamine sulfate	12E11-N06	2
Fagron	Amphetamine sulfate	13B11-N04	2
Fagron	Amphetamine sulfate	13D09-N03	1
Fagron	Amphetamine sulfate	88689	2
Fagron	Amphetamine sulfate	15L01-B05-315291	3
Fagron	Amphetamine sulfate	16A29-B03	8
Fagron	Amphetamine sulfate	16A29B03318744	1
Fagron	Amphetamine sulfate	15101-b05-315292	1
Fagron	Amphetamine sulfate	96200	1
Fagron	Amphetamine sulfate	324577	2
Fagron	Amphetamine sulfate	315291	1
Fagron	Amphetamine sulfate	16A29-B03-324578	3
Fagron	Amphetamine sulfate	17K03-B01-344122	1
Fagron	Amphetamine sulfate	78012	1
Fagron	Amphetamine sulfate	16A29-B03-318743	6
Fagron	Amphetamine sulfate	16A29_B03_318744	1
Fagron	Amphetamine sulfate	11/01-N01	1
Fagron	Amphetamine sulfate	16A29-B03-328317	5
Fagron	Amphetamine sulfate	2213Q-03361	1
Fagron	Amphetamine sulfate	11D04-N13	1
Fagron	Amphetamine sulfate	13J18B40	1
Fagron	Amphetamine sulfate	16a29-b03-318744	2
Fagron	Amphetamine sulfate	12/24N-03	1
Fagron	Amphetamine sulfate	13G08-N11	3
Fagron	Amphetamine sulfate	13J18-B40	1
Fagron	Amphetamine sulfate	14E19-B09	2
Fagron	Amphetamine sulfate	12B06-N13	2
Fagron	Amphetamine sulfate	15L01-B05-315290	1
Fagron	Amphetamine sulfate	13J18-B40-290538	1
Fagron	Amphetamine sulfate	14E19-B09-304502	2
Fagron	Amphetamine sulfate	16K08-B04-336361	1
Gatt Koller/Herba	Amphetamine sulfate	942/03130814	1
Th. Geyer	Amphetamine sulfate	70325	16
Th. Geyer	Amphetamine sulfate	57043	1
Noweda	Amphetamine sulfate	16A29-B03-318744	3
Fagron	Amphetamine sulfate	14E19-B09-294572	1
Phoenix	Amphetamine sulfate	16A29-B03-328317	1
Phönix	Amphetamine sulfate	13B11N04	1
Phönix	Amphetamine sulfate	16a29-b03-328317	1
Sanacorp	Amphetamine sulfate	12/24-N03	1
Th. Geyer	Amphetamine sulfate	PH10051	1
Th. Geyer	Amphetamine sulfate	L0T067043	1
Th. Geyer	Amphetamine sulfate	67043	71
Th. Geyer	Amphetamine sulfate	20170808-03361	1
Th. Geyer	Amphetamine sulfate	6703	1
Th. Geyer	Amphetamine sulfate	21082013B	1
Th. Geyer	Amphetamine sulfate	70525	1
Th. Geyer	Amphetamine sulfate	67002	49
-	Angelica root	130924	1
Bombastus	Angelica root	275879	1
Aurica/Phönix	Angelica root	520800638	1
Bombastus	Angelica root	272895	1
Bombastus	Angelica root	274128	2
Bombastus	Angelica root	269775	2
Bombastus	Angelica root	272954	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Angelica root	270117	1
Bombastus	Angelica root	281280	7
Bombastus	Angelica root	301768	1
Bombastus	Angelica root	290309	1
Bombastus	Angelica root	307041	4
Bombastus	Angelica root	291848	1
Bombastus	Angelica root	295085	2
Bombastus	Angelica root	305460	1
Bombastus	Angelica root	275878	1
Caelo	Angelica root	11093304	1
Caelo	Angelica root	12168703	2
Caelo	Angelica root	12080403	1
Caelo	Angelica root	30011302	1
Caelo	Angelica root	269740	1
Caelo	Angelica root	6081B130109	7
Caelo	Angelica root	10071306	1
Caelo	Angelica root	Int.Ch:318090	1
Caelo	Angelica root	12350705	1
Caelo	Angelica root	5091303	1
Caelo	Angelica root	15101304	1
Caelo	Angelica root	21011402	1
Caelo	Angelica root	12080412	1
Caelo	Angelica root	28101402	1
Caelo	Angelica root	13041711	1
Caelo	Angelica root	17053302	1
Caelo	Angelica root	12168701	3
Caelo	Angelica root	12350703	9
Caelo	Angelica root	12350704	2
Caelo	Angelica root	15162604	2
Caelo	Angelica root	12168705	2
Caelo	Angelica root	14179506	2
Caelo	Angelica root	16128006	1
Caelo	Angelica root	285732	2
Caelo	Angelica root	16128002	2
Caelo	Angelica root	9030301	1
Caelo	Angelica root	303299	1
Caelo	Angelica root	5162606	1
Caelo	Angelica root	17053301	1
Euro OTC	Angelica root	301767	2
gasser	Angelica root	950049	1
Gehe	Angelica root	285732	1
Bombastus	Angelica root	296334/1121115	1
Klenk	Angelica root	6081B130410	4
Klenk	Angelica root	6081N120110	14
Klenk	Angelica root	6081n120110	1
Klenk	Angelica root	B130109	2
Klenk	Angelica root	6091B130109	1
Klenk	Angelica root	6081B130109	1
Klenk	Angelica root	6081B140918	1
Klenk	Angelica root	6081B130726	1
Klenk	Angelica root	6081B150701	7
Klenk	Angelica root		1
Klenk	Angelica root	6081B170601	3
Klenk	Angelica root	6085B120614	1
Klenk	Angelica root	6081b130109	2
Klenk	Angelica root	6082b130410	1
Caelo	Angelica root	17053304	2
Noweda	Angelica root	272720	2
Bombastus	Angelica root	278294	1
Bombastus	Angelica root	278757	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Angelica root	14178506	1
Sanacorp	Angelica root	277310	1
Klenk	Angelica root	6081B160908	1
Weltecke	Angelica root	38011111	1
AHD 10.02.17 EK.3,50	Aniseed	16200801	4
Anzag 06.04.2016	Aniseed	15398601	1
Caelo	Aniseed	1137033	1
Aurica	Aniseed	521302895	1
Bahnhof-Apotheke	Aniseed	7-120913	1
Berkel AHK	Aniseed	11374103	1
Berkel AHK	Aniseed	14194401	1
Bombastus	Aniseed	285778	2
Bombastus	Aniseed	282917	2
Bombastus	Aniseed	289846	2
Bombastus	Aniseed	285777	1
Bombastus	Aniseed	305177	1
Caelo	Aniseed	13037805	11
Caelo	Aniseed	PrüfNr4913E-01530	1
Caelo	Aniseed	13333913	1
Caelo	Aniseed	11101202	3
Caelo	Aniseed	10081207	1
Caelo	Aniseed	11101201	1
Caelo	Aniseed	11101215	3
Caelo	Aniseed	11370303	11
Caelo	Aniseed	10247202	1
Caelo	Aniseed	4061301	1
Caelo	Aniseed	5061301	1
Caelo	Aniseed	13037804	7
Caelo	Aniseed	13037801	1
Caelo	Aniseed	5091304	1
Caelo	Aniseed	13037901	1
Caelo	Aniseed	12360801	1
Caelo	Aniseed	13037808	9
Caelo	Aniseed	13333901	6
Caelo	Aniseed	13333903	3
Caelo	Aniseed	13333902	9
Caelo	Aniseed	5121401	1
Caelo	Aniseed	13333906	3
Caelo	Aniseed	13333909	2
Caelo	Aniseed	13333910	4
Caelo	Aniseed	13333914	1
Caelo	Aniseed	13333916	1
Caelo	Aniseed	15046103	3
Caelo	Aniseed	15046106	1
Caelo	Aniseed	15049103	1
Caelo	Aniseed	16165303	1
Caelo	Aniseed	16165304	4
Caelo	Aniseed	16165302	1
Caelo	Aniseed	15398607	1
Caelo	Aniseed	17045603	1
Caelo	Aniseed	17045601	1
Caelo	Aniseed	16165308	1
Caelo	Aniseed	17045611	2
Caelo	Aniseed	11121705	1
Caelo	Aniseed	13037803	2
Caelo	Aniseed	13037809	12
Caelo	Aniseed	15398605	5
Caelo	Aniseed	15046102	8
Caelo	Aniseed	111101213	1
Caelo	Aniseed	11101213	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Aniseed	15046101	5
Caelo	Aniseed	3314E-01530	1
Caelo	Aniseed	2215M-01530	1
Caelo	Aniseed	2916E-01530	1
Caelo	Aniseed	15283201	3
Caelo	Aniseed	11370301	10
Caelo	Aniseed	13333908	7
Caelo	Aniseed	11370308	3
Caelo	Aniseed	15398603	4
Caelo	Aniseed	16165306	5
Caelo	Aniseed		1
Caelo	Aniseed	11101203	6
Caelo	Aniseed	13037807	2
Caelo	Aniseed	11370302	4
Caelo	Aniseed	12226402	5
Caelo	Aniseed	140913a	1
Caelo	Aniseed	13333907	4
Caelo	Aniseed	17045608	1
Caelo	Aniseed	17045609	1
Caelo	Aniseed	15046109	5
Caelo	Aniseed	15046110	1
Caelo	Aniseed	13037808-3560412014	1
Caelo	Aniseed	16165305	5
Caelo	Aniseed	15398602	5
Caelo	Aniseed	13333912	3
Caesar & Loretz/Noweda	Aniseed	153986002	1
Fagron	Aniseed	11370304	6
galke	Aniseed	19654	1
Galke	Aniseed	21278	1
Galke	Aniseed	22274	1
Galke	Aniseed	23464	1
GALKE	Aniseed	29047	1
Gehe	Aniseed	10247203	1
Gutenberg-Apotheke	Aniseed	1333902	1
Hepart AG	Aniseed	B216346, kbA	1
Jenne	Aniseed	2700A131015	2
Klenk	Aniseed	212M-01530	1
Klenk	Aniseed	2700A110701	7
Klenk	Aniseed	2901311530	1
Klenk	Aniseed	2103311530	1
Klenk	Aniseed	3113Q01530	1
Klenk	Aniseed	2700A130527	14
Klenk	Aniseed	2700A160511	6
Klenk	Aniseed	2700A150810	2
Klenk	Aniseed	2700A170803	1
Klenk	Aniseed	2700A190107	1
Klenk	Aniseed	2700A-110701	1
Klenk	Aniseed	2700A120320	8
Klenk	Aniseed	2700a120320	1
Klenk	Aniseed	2700A150901	1
Klenk	Aniseed	2700A140129	6
Klenk	Aniseed	2700A12107	1
Klenk	Aniseed	814Q01530	1
Klenk	Aniseed	2700A121107	1
Klenk	Aniseed	2700A150601	7
nachprüfung	Aniseed	C1246	1
Nachprüfung	Aniseed	5010U-01530	1
Caelo	Aniseed	13037802	9
Caelo	Aniseed	11101214	6
siehe Protokoll	Aniseed	sieheProtokoll	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Wolf	Aniseed	215346	1
Wolf	Aniseed	B216346	14
Wolf	Aniseed	216346	1
Wolf	Aniseed	B-671	2
Wolf	Aniseed	B671	1
Wolf	Aniseed	L401F292b	4
Wolf	Aniseed	L401F1413	1
Caelo	Aniseed, pounded	12111304	1
Caelo	Aniseed, pounded	11242003	1
Caelo	Aniseed, pounded	4041302	1
Caelo	Aniseed, pounded	23041303	1
Caelo	Aniseed, pounded	15149702	1
Caelo	Aniseed, pounded	1314990	1
Caelo	Aniseed, pounded	12111303	3
Gahlke	Aniseed, pounded	21401	1
Gehe	Aniseed, pounded	13149903	1
Caelo	Aniseed, pounded	13149902	1
Caelo	Aniseed, pounded	12360803	2
Klenk	Aniseed, pounded	2706B100120	1
Aurica Naturheilmitte...	Aniseed, powdered	521405796	1
Klenk	Aniseed, powdered	2704B110824	1
vedono	Aniseed, powdered	11306208	1
Caelo	Apple, cut	12227301	1
Klenk	Apple, cut	A120302	3
Caelo	Arnica flower	10207405	1
Caelo	Arnica flower	28071201	1
Caelo	Arnica flower	10081204	1
Caelo	Arnica flower	11259804	1
Caelo	Arnica flower	12227202	1
Caelo	Arnica flower	12227202	1
Caelo	Arnica flower	IntCh:212032	1
Caelo	Arnica flower	11285705	1
Caelo	Arnica flower	11259803	1
Caelo	Arnica flower	11285703	1
Caelo	Arnica flower	6112013A	1
Caelo	Arnica flower	12227203	1
Caelo	Arnica flower	1222702	1
Caelo	Arnica flower	11374105	1
Caelo	Arnica flower	11374103	1
Caelo	Arnica flower	11374101	2
Caelo	Arnica flower	11374102	2
Gehe	Arnica flower	11259801	2
Klenk	Arnica flower	1181B130605	1
Bombastus	Artichoke leaf, cut	8202213593	1
Caelo	Artichoke leaf, cut	12173302	3
Caelo	Artichoke leaf, cut	12173304	3
Caelo	Artichoke leaf, cut	12173307	6
Caelo	Artichoke leaf, cut	2312I-03593	1
Caelo	Artichoke leaf, cut	12173306	2
Caelo	Artichoke leaf, cut	13037607	4
Caelo	Artichoke leaf, cut	13037608	1
Caelo	Artichoke leaf, cut	13037603	1
Caelo	Artichoke leaf, cut	81232298	1
Caelo	Artichoke leaf, cut	12173307-3260315072	1
Caelo	Artichoke leaf, cut	13310706	1
Kenk / Phoenix	Artichoke leaf, cut	1981B130111	3
Klenk	Artichoke leaf, cut	B121025	2
Klenk	Artichoke leaf, cut	1981B121025	2
Klenk	Artichoke leaf, cut	1981B120413	1
Caelo	Ash leaf, cut	12225504	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Ash leaf, cut	12225502	1
Caelo	Ash leaf, cut	12225505	2
Klenk	Ash leaf, cut	5111A-01491	1
Caelo	Asparagus root, cut	13193302	1
Caelo	Asparagus root, cut	13193308	1
Galke	Asparagus root, cut	20178	1
Caelo	Asparagus root, cut	13071002	1
Klenk	Asparagus root, cut	6151B100332	1
Klenk	Asplenium scolopendri...	4451B091116	1
Klenk	Asplenium scolopendri...	4451B120605	1
Caelo	Barberries	11058320	1
Caelo	Barberries	12217103	3
Caelo	Barberries	12217106	1
Caelo	Barberries	12217111	1
Caelo	Barberries	12217113	2
Caelo	Barberries	12217116	1
Caelo	Barberries	16224202	1
Caelo	Barberries	12217107	1
Caelo	Barberries	1221707	1
Caelo	Barberries	12217109	4
Caelo	Barberry root bark, cut	11083509	1
Caelo	Barberry root bark, cut	55B110128	1
Caelo	Barberry root bark, cut	12112606	5
Caelo	Barberry root bark, cut	12112603	2
Caelo	Barberry root bark, cut	12112605	1
Klenk	Barberry root bark, cut	551B110128	4
Klenk	Barberry root bark, cut	551B120320	1
Caelo	Barberry root bark, cut	12112608	1
Fagron	Barbital sodium	15L07-B02	1
Klenk	Basil, rubbed	3632A110201	3
Caelo	Basil, rubbed	12066404	1
Caelo	Basil, rubbed	12007010	4
Caelo	Basil, rubbed	12007008	2
Caelo	Basil, rubbed	13048601	2
Caelo	Basil, rubbed	13048605	1
Caelo	Basil, rubbed	13048605-3519411022	1
Klenk	Basil, rubbed	3632A120502	4
Klenk	Basil, rubbed	A110201	1
Klenk	Basil, rubbed	A120502	1
Klenk	Basil, rubbed	3632a120502	1
VDL	Basil, rubbed	12007004	1
Aurica/Phönix	Bean shells, cut	5052301	1
Bombastus	Bean shells, cut	272781	3
Bombastus	Bean shells, cut	278686	1
Bombastus	Bean shells, cut	282475	1
Bombastus	Bean shells, cut	278696	2
Bombastus	Bean shells, cut	270517	1
Bombastus	Bean shells, cut	240503	1
Cae	Bean shells, cut	Int.Ch.313011	1
Caelo	Bean shells, cut	29091201	1
Caelo	Bean shells, cut	8301004	1
Caelo	Bean shells, cut	6031301	1
Caelo	Bean shells, cut	11030604	6
Caelo	Bean shells, cut	1103061	1
Caelo	Bean shells, cut	11030601	1
Caelo	Bean shells, cut	13333801	1
Caelo	Bean shells, cut	1333802	1
Caelo	Bean shells, cut	13333803	1
Caelo	Bean shells, cut	14080002	1
Caelo	Bean shells, cut	15060905	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Bean shells, cut	12358703	5
Caelo	Bean shells, cut	10006507	1
Caelo	Bean shells, cut	11233603	1
Caelo	Bean shells, cut	11030602	5
Caelo	Bean shells, cut	11030605	1
Galke	Bean shells, cut	21219	1
Klenk	Bean shells, cut	671A100816	2
Klenk	Bean shells, cut	171A110301	1
Klenk	Bean shells, cut	C120321	2
Klenk	Bean shells, cut	671C121105	8
Klenk	Bean shells, cut	C121105	2
Klenk	Bean shells, cut	671C130620	6
Klenk	Bean shells, cut	C130620	1
Klenk	Bean shells, cut	671A110420	9
Klenk	Bean shells, cut	671A-110420	1
Klenk	Bean shells, cut	671A110301	1
Klenk	Bean shells, cut	671C120321	16
Caelo	Bearberry leaf, cut	12186506	3
Bombastus	Bearberry leaf, cut	272297	8
Bombastus	Bearberry leaf, cut	275491	3
Bombastus	Bearberry leaf, cut	267926	1
Caelo	Bearberry leaf, cut	11213011	3
Caelo	Bearberry leaf, cut	20111210	1
Caelo	Bearberry leaf, cut	11213010	1
Caelo	Bearberry leaf, cut	13067802	3
Caelo	Bearberry leaf, cut	12186503	1
Caelo	Bearberry leaf, cut	15051303	1
Caelo	Bearberry leaf, cut	4091301	1
Caelo	Bearberry leaf, cut	13067805	6
Caelo	Bearberry leaf, cut	5111301	1
Caelo	Bearberry leaf, cut	12186504	1
Caelo	Bearberry leaf, cut	17121306	1
Caelo	Bearberry leaf, cut	4021407	1
Caelo	Bearberry leaf, cut	15116201	1
Caelo	Bearberry leaf, cut	1218602	1
Caelo	Bearberry leaf, cut	280889	3
Caelo	Bearberry leaf, cut	11213005	4
Caelo	Bearberry leaf, cut	412A-01518	1
Caelo	Bearberry leaf, cut	13067805-3390311080	1
Klenk	Bearberry leaf, cut	2391b120314	2
Galke	Bearberry leaf, cut	19936	3
Klenk	Bearberry leaf, cut	2391B120314	6
Klenk	Bearberry leaf, cut	2391B130328	9
Klenk	Bearberry leaf, cut	2391B07030901	1
Caelo	Bearberry leaf, cut	12186502	1
Sanacorp	Bearberry leaf, cut	2391B110209	3
Klenk	Bearberry leaf, cut	2391B120719	13
Caelo	Bentonite	fürHerrSalloch	1
Caelo	Bentonite	1307016-01	1
Caelo	Bentonite	1311014-01	1
Clariant - Mindel-Food	Bentonite	1301	1
Noweda	Bentonite	11304415	1
Euro OTC	Betaine hydrochloride	1202008-01	1
Euro OTC	Betaine hydrochloride	L1701040-01	1
Euro OTC	Betaine hydrochloride	1305027-01	2
Euro OTC	Betaine hydrochloride	L1510011-03	2
Euro OTC	Betaine hydrochloride	1510011-02	1
Euro OTC	Betaine hydrochloride	L1412019-01	1
Fagron	Betaine hydrochloride	12C20-N09	1
Fagron	Betaine hydrochloride	24091301	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Betaine hydrochloride	15121401	1
Gatt-Koller	Betaine hydrochloride	2970/07102910	1
Fagron	Betaine hydrochloride	13G29-B02-294870	1
Caelo	Betamethasone-17-vale...	12A05-N08	3
Caelo	Betamethasone-17-vale...	12a05-no8	1
Fagron	Betamethasone-17-vale...	12a05-n08	1
Fagron	Betamethasone-17-vale...	12G02-N02	2
Fagron	Betamethasone-17-vale...	12C19-N07	1
Fagron	Betamethasone-17-vale...	12L19-N06	4
Fagron	Betamethasone-17-vale...	12J19-N06	1
Fagron	Betamethasone-17-vale...	13E08-N01	1
Fagron	Betamethasone-17-vale...	12G02-N15	3
Bombastus	Betony herb, cut	12007205	2
Caelo	Betony herb, cut	12007208	1
Caelo	Betony herb, cut	13048906	1
Caelo	Betony herb, cut	134048903	1
Caelo	Betony herb, cut	13367802	1
Sanacorp	Betony herb, cut	13048903	3
Caelo	Betony herb, cut	12007201	1
Anzag	Bilberry fruit, dried	2910N120921	2
Cae	Bilberry fruit, dried	212172	1
Caelo	Bilberry fruit, dried	13130504	1
Caelo	Bilberry fruit, dried	12183701	2
Caelo	Bilberry fruit, dried	26061301	1
Caelo	Bilberry fruit, dried	10265601	1
Caelo	Bilberry fruit, dried	18101307	1
Caelo	Bilberry fruit, dried	13130501	1
Caelo	Bilberry fruit, dried	10273708	1
Caelo	Bilberry fruit, dried	10273709	1
Caelo	Bilberry fruit, dried	10265603	1
Caelo	Bilberry fruit, dried	10273711	1
Caelo	Bilberry fruit, dried	12183704	4
Fiebig 05.11.12 ek:9...	Bilberry fruit, dried	2910A120410	1
Klenk	Bilberry fruit, dried	2910N110304	5
Klenk	Bilberry fruit, dried	2010N110304	1
Klenk	Bilberry fruit, dried	2910A090717	1
Klenk	Bilberry fruit, dried	2910N130131	11
Klenk	Bilberry fruit, dried	N130131	2
Klenk	Bilberry fruit, dried	N121022	1
Klenk	Bilberry fruit, dried	2910n130131	1
Klenk	Bilberry fruit, dried	910N130131	1
Klenk	Bilberry fruit, dried	2910n110304	1
Klenk	Bilberry fruit, dried	2910N121022	7
Bombastus	Bilberry leaf, cut	272176	2
Caelo	Bilberry leaf, cut	13009904	3
Caelo	Bilberry leaf, cut	9367603	2
Caelo	Bilberry leaf, cut	23111201	1
Caelo	Bilberry leaf, cut	12140206	2
Caelo	Bilberry leaf, cut	3091302	1
Caelo	Bilberry leaf, cut	13009907	2
Caelo	Bilberry leaf, cut	12140201	2
Caelo	Bilberry leaf, cut	13009901	3
Caelo	Bilberry leaf, cut	13009903	4
Caelo	Bilberry leaf, cut	1300907	1
Klenk	Bilberry leaf, cut	4042013	1
Klenk	Bilberry leaf, cut	2191N110516	5
Klenk	Bilberry leaf, cut	N110516	1
Sanacorp	Bilberry leaf, cut	2191A130410	2
Caelo	Bilberry leaf, cut	12140204	4
Aurica	Birch leaf, cut	521205644	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bahnhof-Apotheke	Birch leaf, cut	18-120702	1
Bombastus	Birch leaf, cut	280677	1
Bombastus	Birch leaf, cut	287280	1
Bombastus	Birch leaf, cut	272385	1
Bombastus	Birch leaf, cut	267077	1
Bombastus	Birch leaf, cut	270743	1
Caelo	Birch leaf, cut	11189510	3
Caelo	Birch leaf, cut	11189507	1
Caelo	Birch leaf, cut	11189508	1
Caelo	Birch leaf, cut	12193109	15
Caelo	Birch leaf, cut	IntCh:311092	1
Caelo	Birch leaf, cut	12193108	1
Caelo	Birch leaf, cut	13108906	1
Caelo	Birch leaf, cut	13337303	1
Caelo	Birch leaf, cut	13337302	1
Caelo	Birch leaf, cut	13108917	1
Caelo	Birch leaf, cut	14360702	1
Caelo	Birch leaf, cut	13108916	1
Caelo	Birch leaf, cut	12193104	1
Caelo	Birch leaf, cut	107063	1
Caelo	Birch leaf, cut	11189502	1
Caelo	Birch leaf, cut	12193004	5
Caelo	Birch leaf, cut	12193105	3
Caelo	Birch leaf, cut	13337303-3561412013	1
Caesar & Loretz GmbH,...	Birch leaf, cut	11050102	3
Fagron	Birch leaf, cut	7061301	1
Galke	Birch leaf, cut	20904	1
Galke	Birch leaf, cut	21226	1
Klenk	Birch leaf, cut	1901A110726	24
Klenk	Birch leaf, cut	1901c120508	1
Klenk	Birch leaf, cut	20111201	1
Klenk	Birch leaf, cut	1901C120508	18
Klenk	Birch leaf, cut	F-040413-1	1
Klenk	Birch leaf, cut	C120802	1
Klenk	Birch leaf, cut	21061303	1
Klenk	Birch leaf, cut	A121130	2
Klenk	Birch leaf, cut	1901A121130	24
Klenk	Birch leaf, cut	1901c120802	1
Klenk	Birch leaf, cut	28101306	1
Klenk	Birch leaf, cut	27121301	1
Klenk	Birch leaf, cut	1901A130218	5
Klenk	Birch leaf, cut	4021409	1
Klenk	Birch leaf, cut	1901A130318	2
Klenk	Birch leaf, cut	1901A140214	1
Klenk	Birch leaf, cut	1901A-110726	3
Klenk	Birch leaf, cut	1901C120802	19
Klenk	Birch leaf, cut	4213I01481	1
Klenk	Birch leaf, cut	1901A05051801	1
Klenk	Birch leaf, cut	4113A-01481	1
Caelo	Birch leaf, cut	13108905	8
Spangropharm	Birch leaf, cut	264603	1
AHD	Bitter fennel	15006502	1
AHD;11.05.15;3,23	Bitter fennel	14376408	3
Alfred Galke	Bitter fennel	18270	1
Bahnhof-Apotheke	Bitter fennel	11-121029	1
Bombastus	Bitter fennel	268130	2
Bombastus	Bitter fennel	285609	1
Bombastus	Bitter fennel	296877	3
Bombastus	Bitter fennel	299386	3
Bombastus	Bitter fennel	289870	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Bitter fennel	299385	3
Bombastus	Bitter fennel	280891	2
Bombastus	Bitter fennel	289870	1
Bombastus	Bitter fennel	289869	2
Bombastus	Bitter fennel	293627	1
Bombastus	Bitter fennel	275922	4
Cae	Bitter fennel	Int.Ch.314090	1
Caelo	Bitter fennel	16061202	1
Caelo	Bitter fennel	11185501	1
Caelo	Bitter fennel	6091201	1
Caelo	Bitter fennel	12094703	2
Caelo	Bitter fennel	1209474	1
Caelo	Bitter fennel	12035102	2
Caelo	Bitter fennel	27121201	1
Caelo	Bitter fennel	12167102	4
Caelo	Bitter fennel	11016330	1
Caelo	Bitter fennel	402311545	1
Caelo	Bitter fennel	12094712	4
Caelo	Bitter fennel	12094716	7
Caelo	Bitter fennel	7031306	1
Caelo	Bitter fennel	13020802	6
Caelo	Bitter fennel	12094720	7
Caelo	Bitter fennel	4061302	1
Caelo	Bitter fennel	5061302	1
Caelo	Bitter fennel	12094721	3
Caelo	Bitter fennel	12094719	4
Caelo	Bitter fennel	12094724	4
Caelo	Bitter fennel	13200401	4
Caelo	Bitter fennel	14111301	1
Caelo	Bitter fennel	13148303	2
Caelo	Bitter fennel	12362710	1
Caelo	Bitter fennel	13148305	3
Caelo	Bitter fennel	9121305	1
Caelo	Bitter fennel	13200402	2
Caelo	Bitter fennel	13148306	1
Caelo	Bitter fennel	13371605	1
Caelo	Bitter fennel	13371610	1
Caelo	Bitter fennel	13371610	2
Caelo	Bitter fennel	13398502	1
Caelo	Bitter fennel	5121401	1
Caelo	Bitter fennel	13398502	1
Caelo	Bitter fennel	14376405	1
Caelo	Bitter fennel	15006507	1
Caelo	Bitter fennel	15443203	2
Caelo	Bitter fennel	15443205	2
Caelo	Bitter fennel	15443209	3
Caelo	Bitter fennel	15443202	3
Caelo	Bitter fennel	154443204	1
Caelo	Bitter fennel	15443213	1
Caelo	Bitter fennel	16298101	1
Caelo	Bitter fennel	17341502	1
Caelo	Bitter fennel	12094710	4
Caelo	Bitter fennel	14255802	3
Caelo	Bitter fennel	12167101	1
Caelo	Bitter fennel	12094715	4
Caelo	Bitter fennel	12345678	1
Caelo	Bitter fennel	16005902	1
Caelo	Bitter fennel	15443215	4
Caelo	Bitter fennel	15007601	1
Caelo	Bitter fennel	14376408;21S08	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Bitter fennel	13148304	24
Caelo	Bitter fennel	12094717	1
Caelo	Bitter fennel	12035102	1
Caelo	Bitter fennel	12094726	2
Caelo	Bitter fennel	15141004	1
Caelo	Bitter fennel	15443208	2
Caelo	Bitter fennel	15443212	3
Caelo	Bitter fennel	1302081	1
Caelo	Bitter fennel	13020801	4
Caelo	Bitter fennel	1320041	1
Caelo	Bitter fennel	13148307	1
Caelo	Bitter fennel	15006501	2
Caelo	Bitter fennel	15443206	1
Caelo	Bitter fennel	14376406	2
Caelo	Bitter fennel	14376402	1
Caelo	Bitter fennel	15006508	3
Caelo	Bitter fennel	15443204	7
Caelo	Bitter fennel	12094716-3408310191	1
Caelo	Bitter fennel	13148304-3500411070	1
Caelo	Bitter fennel	14376401	2
Caelo	Bitter fennel	16298102	1
Caesar & Loretz GmbH ...	Bitter fennel	11016331	1
Caesar & Loretz GmbH,...	Bitter fennel	11016319	1
Caesar & Loretz GmbH,...	Bitter fennel	12094705	4
Caesar & Loretz GmbH,...	Bitter fennel	12094705	2
Caesar & Loretz GmbH,...	Bitter fennel	12094707	6
Caesar & Loretz GmbH,...	Bitter fennel	12094711	2
Caesar & Loretz GmbH,...	Bitter fennel	12094725	8
Defektur	Bitter fennel	7/13	1
Defektur	Bitter fennel	52/13	1
Defektur	Bitter fennel	57/13	1
Fagron	Bitter fennel	1406211545	1
Fagron	Bitter fennel		1
Fagron	Bitter fennel	6858913	1
Gahlke	Bitter fennel	20362	1
galke	Bitter fennel	19938	3
Galke	Bitter fennel	22176	1
GALKE	Bitter fennel	27755	1
Gehe	Bitter fennel	2860A120412	24
Caelo	Bitter fennel	1250117/15443216	1
Hepart AG	Bitter fennel	B492, kBA	1
Klenk	Bitter fennel	2860A110704	4
Klenk	Bitter fennel	3812A-01545	1
Klenk	Bitter fennel	2880N120418	4
Klenk	Bitter fennel	2860A140224	1
Klenk	Bitter fennel	2860A140612	15
Klenk	Bitter fennel	2860A140224	1
Klenk	Bitter fennel	2860A130513	2
Klenk	Bitter fennel	2860A150617	5
Klenk	Bitter fennel	2860A150320	13
Klenk	Bitter fennel	2866B100211	1
Klenk	Bitter fennel	2866B130206	1
Klenk	Bitter fennel	2866B110318	1
Klenk	Bitter fennel	2860A160606	1
Klenk	Bitter fennel	2860, A150617	1
Klenk	Bitter fennel	2860A140613	2
Klenk	Bitter fennel	28060A140612	1
Klenk	Bitter fennel	2860a120412	3
Kottas	Bitter fennel	P15301479	1
Noweda	Bitter fennel	2860A180212	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Noweda 06.04.2016	Bitter fennel	15443201	1
Caelo	Bitter fennel	12094704	4
Phönix	Bitter fennel	12094708	2
Caelo	Bitter fennel	2150317	1
Klenk	Bitter fennel	2880A100503	2
Caelo	Bitter fennel	15006506	1
Caelo	Bitter fennel	15443216	1
Caelo	Bitter fennel	17020603	1
siehe Protokoll (Galke)	Bitter fennel	sieheProtokoll	2
Spangro/gepepharm	Bitter fennel	15007602	2
Klenk	Bitter fennel	2860A130226	8
Wolf	Bitter fennel	B-362	1
Wolf	Bitter fennel	B362	2
Wolf	Bitter fennel	B-493	1
Wolf	Bitter fennel	B-682	1
Wolf	Bitter fennel	B382	1
Wolf	Bitter fennel	B492	1
Wolf	Bitter fennel	B-492	5
-	Bitter orange flower ...	2011A-01445	1
Caelo	Bitter orange flower ...	11049212	1
Caelo	Bitter orange flower ...	12266703	2
Caelo	Bitter orange flower ...	11049202	1
Caelo	Bitter orange flower ...	12266608	6
Caelo	Bitter orange flower ...	2712E-01445	1
Caelo	Bitter orange flower ...	12266609	1
Caelo	Bitter orange flower ...	6051301	1
Caelo	Bitter orange flower ...	12266708	1
Caelo	Bitter orange flower ...	13067903	2
Caelo	Bitter orange flower ...	12266705	1
Caelo	Bitter orange flower ...	12266614	1
Caelo	Bitter orange flower ...	13352701	1
Caelo	Bitter orange flower ...	12266707	1
Caelo	Bitter orange flower ...	12266605	1
Caelo	Bitter orange flower ...	12266611	1
Caelo	Bitter orange flower ...	12266608	2
Caelo	Bitter orange flower ...	12266605	1
Caelo	Bitter orange flower ...	12266611	1
Caelo	Bitter orange flower ...	13352701-3518411022	1
Hepart AG	Bitter orange flower ...	B120822	1
Klenk	Bitter orange flower ...	1201B120822	1
Klenk	Bitter orange flower ...	1201B110809	1
Klenk	Bitter orange flower ...	3613m-01445	1
Bombastus	Bitter orange peel, cut	278233	4
Bombastus	Bitter orange peel, cut	274240	3
Caelo	Bitter orange peel, cut	12239203	3
Caelo	Bitter orange peel, cut	12067402	1
Caelo	Bitter orange peel, cut	17111201	1
Caelo	Bitter orange peel, cut	12067405	1
Caelo	Bitter orange peel, cut	4312M-01531	1
Caelo	Bitter orange peel, cut	13049001	1
Caelo	Bitter orange peel, cut	21101302	1
Caelo	Bitter orange peel, cut	27011403	1
Klenk	Bitter orange peel, cut	511B110321	2
Klenk	Bitter orange peel, cut	2711B111207	1
Klenk	Bitter orange peel, cut	511B120830	4
Klenk	Bitter orange peel, cut	511A110411	1
Klenk	Bitter orange peel, cut	B120830	1
Klenk	Bitter orange peel, cut	C130226	3
Klenk	Bitter orange peel, cut	511C130226	1
Klenk	Bitter orange peel, cut	3613M-01531	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
kräuter schulte	Bitter orange peel, cut	51265	1
Caelo	Black cohosh, cut	10281112	1
Caelo	Black cohosh, cut	10281104	1
Caelo	Black cohosh, cut	10281118	2
Caelo	Black cohosh, cut	13142101	1
Caelo	Black cohosh, cut	13237903	1
Klenk	Black cohosh, cut	6721B141202	1
Caelo	Black cohosh, cut	13237901	2
Klenk	Black cohosh, cut	6721B130214	10
Klenk	Black cohosh, cut	B130528	2
Klenk	Black cohosh, cut	6721B1130528	1
Klenk	Black cohosh, cut	3794377	1
Klenk	Black cohosh, cut	6721B081208	1
Klenk	Black cohosh, cut	6721b130528	1
Kräuter Schulte	Black cohosh, cut	3308M-02176	1
Nachprüfung	Black cohosh, cut	10281113	1
Klenk	Black cohosh, cut	6721B130528	3
Akazie	Black cumin seed	20.09.2015	1
Caelo	Black cumin seed	10121916	1
Caelo	Black cumin seed	10121915	1
Caelo	Black cumin seed	11233502	2
Caelo	Black cumin seed	12358901	2
Caelo	Black cumin seed	12358906	2
Caelo	Black cumin seed	13326405	2
Caelo	Black cumin seed	13326406	1
Caelo	Black cumin seed	14359903	3
Caelo	Black cumin seed	14359905	1
Caelo	Black cumin seed	12358903	2
Caelo	Black cumin seed	16115708	3
Caelo	Black cumin seed	15300401	3
Caelo	Black cumin seed	16115706	1
Caelo	Black cumin seed	11233507	1
Caelo	Black cumin seed	13122013b	1
Caelo	Black cumin seed	16115703	2
Chiesi/Phönix	Black cumin seed	14359906	2
Hepart AG	Black cumin seed	20720, kBA	1
Caelo	Black cumin seed	12358902	1
Caelo	Black cumin seed	12358904	1
Klenk	Black cumin seed	7330A120703	1
Klenk	Black cumin seed	A120703	1
Caelo	Black cumin seed	11233503	1
Spinnrad	Black cumin seed	11931059	1
Spinnrad/Phoenix	Black cumin seed	613310592	1
Wolf	Black cumin seed		1
Wolf	Black cumin seed	20720	8
Wolf	Black cumin seed	B-471	1
Wolf	Black cumin seed	207204	1
Wolf	Black cumin seed	L310F141b	6
Wolf	Black cumin seed	L402F1713	1
Wolf	Black cumin seed	L402F171b	3
Caelo	Black mustard seed	12189307	1
Caelo	Black mustard seed	14057702	1
Caelo	Black mustard seed	16139102	1
Caelo	Black mustard seed	13038904	1
Klenk	Black mustard seed	7430A120813	2
Caelo	Black mustard seed, p...	17196303	4
Klenk	Black mustard seed, p...	7434A120712	1
Caelo	Black mustard seed, p...	16051810	4
Caelo	Black mustard seed, p...	12009702	4
Caelo	Black mustard seed, p...	12009706	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Black mustard seed, p...	12208602	5
Caelo	Black mustard seed, p...	12208601	3
Caelo	Black mustard seed, p...	12350202	16
Caelo	Black mustard seed, p...	12350208	7
Caelo	Black mustard seed, p...	12350204	2
Caelo	Black mustard seed, p...	12350210	1
Caelo	Black mustard seed, p...	12350211	3
Caelo	Black mustard seed, p...	13097705	6
Caelo	Black mustard seed, p...	12350209	1
Caelo	Black mustard seed, p...	13097704	4
Caelo	Black mustard seed, p...	13358302	13
Caelo	Black mustard seed, p...	25011401	1
Caelo	Black mustard seed, p...	13358304	4
Caelo	Black mustard seed, p...	23061401	1
Caelo	Black mustard seed, p...	14162810	2
Caelo	Black mustard seed, p...	14293702	6
Caelo	Black mustard seed, p...	14162802	1
Caelo	Black mustard seed, p...	15131102	3
Caelo	Black mustard seed, p...	15214703	1
Caelo	Black mustard seed, p...	15214707	1
Caelo	Black mustard seed, p...	15214713	2
Caelo	Black mustard seed, p...	16051807	1
Caelo	Black mustard seed, p...	12350205	2
Caelo	Black mustard seed, p...	12208604	3
Caelo	Black mustard seed, p...	11276701	1
Caelo	Black mustard seed, p...	12009703	1
Caelo	Black mustard seed, p...	15214714	1
Caelo	Black mustard seed, p...	16051807	1
Caelo	Black mustard seed, p...	15131101	1
Caelo	Black mustard seed, p...	16272704	2
Caelo	Black mustard seed, p...	14293706	1
Caelo	Black mustard seed, p...	15214707	1
Caelo	Black mustard seed, p...	13097701	11
Caelo	Black mustard seed, p...	13097702	4
Caelo	Black mustard seed, p...	2015Q-02244	1
Caelo	Black mustard seed, p...	17196306	1
Caelo	Black mustard seed, p...	14162807	3
Caelo	Black mustard seed, p...	14162810	3
Caelo	Black mustard seed, p...	14245601	1
Caelo	Black mustard seed, p...	14293701	2
Caelo	Black mustard seed, p...	14293710	2
Caelo	Black mustard seed, p...	15131104	1
Caelo	Black mustard seed, p...	15214703	4
Caelo	Black mustard seed, p...	16051802	2
Caelo	Black mustard seed, p...	16272703	6
Caelo	Black mustard seed, p...	16272707	3
Caelo	Black mustard seed, p...	16333501	2
Caelo	Black mustard seed, p...	1633503	1
Caelo	Black mustard seed, p...	17196301	1
Caelo	Black mustard seed, p...	15131105	1
Caelo	Black mustard seed, p...	15214706	3
Caelo	Black mustard seed, p...	14162808	1
Caelo	Black mustard seed, p...	14293713	1
Caelo	Black mustard seed, p...	15214708	4
Caelo	Black mustard seed, p...	12350202-3369319012	1
Caelo	Black mustard seed, p...	13097706	2
Caelo	Black mustard seed, p...	12350207	5
Caesar/ Noweda	Black mustard seed, p...	14293711	3
Caelo	Black mustard seed, p...	16333503	2
Caelo	Black mustard seed, p...	17276404	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Black mustard seed, p...	A130422	1
Klenk	Black mustard seed, p...	7434A130422	3
Klenk	Black mustard seed, p...	7434A140923	2
Klenk	Black mustard seed, p...	7434A150608	4
Klenk	Black mustard seed, p...	7434a150608	1
Noweda/Henry Lamotte	Black mustard seed, p...	1493708	1
Caelo	Black pepper	11193911	1
Caelo	Black pepper	12192304	1
Caelo	Black pepper	12192306	1
Caelo	Black pepper	12192305	1
Caelo	Black pepper	12192309	1
Caelo	Black pepper	15395310	1
Caelo	Black pepper	13221110	1
Klenk	Black pepper	A130415	2
PHOENIX 19.05.2014	Black pepper	13221105	1
Anzag	Blackberry leaf, cut	10136412	1
Anzag 27.12.12 ek:2,79	Blackberry leaf, cut	10136048	1
Bahnhof-Apotheke	Blackberry leaf, cut	18-120702	1
Bombastus	Blackberry leaf, cut	267122	1
Bombastus	Blackberry leaf, cut	273668	2
Caelo	Blackberry leaf, cut	2271c120508	1
Caelo	Blackberry leaf, cut	10136403	1
Caelo	Blackberry leaf, cut	10136408	6
Caelo	Blackberry leaf, cut	28061202	1
Caelo	Blackberry leaf, cut	13091206	1
Caelo	Blackberry leaf, cut	11030704	4
Caelo	Blackberry leaf, cut	11030707	5
Caelo	Blackberry leaf, cut	3011E-01512	1
Caelo	Blackberry leaf, cut	11030706	1
Caelo	Blackberry leaf, cut	3091303	1
Caelo	Blackberry leaf, cut	14111318	1
Caelo	Blackberry leaf, cut	13127901	1
Caelo	Blackberry leaf, cut	13101610	1
Caelo	Blackberry leaf, cut	14019010	1
Caelo	Blackberry leaf, cut	15039301	1
Caelo	Blackberry leaf, cut	11030701	2
Gehe	Blackberry leaf, cut	10136409	1
Klenk	Blackberry leaf, cut	2271B111216	1
Caelo	Blackcurrant leaf, cut	9373913	1
Caelo	Blackcurrant leaf, cut	12115902	1
Caelo	Blackcurrant leaf, cut	12168804	1
Caelo	Blackcurrant leaf, cut	12168810	3
Caelo	Blackcurrant leaf, cut	80558228	1
Klenk	Blackcurrant leaf, cut	2251a110204	1
Nachprüfung	Blackcurrant leaf, cut	1003	1
Sanacorp	Blackcurrant leaf, cut	2251A110204	4
Caelo	Blackcurrants	12272804	3
Galke	Blackcurrants	21348	1
Klenk	Blackcurrants	A121106	1
Klenk	Blackcurrants	2990A110620	1
Caelo	Blackthorn flower	11206906	1
Caelo	Blackthorn flower	12178104	4
Caelo	Blackthorn flower	12178105	1
Caelo	Blackthorn flower	12178102	9
Caelo	Blackthorn flower	12178103	2
Caelo	Blackthorn flower	12178101	1
Klenk	Blackthorn flower	2612E-01468	1
Caelo	Blackthorn flower, ru...	1150N101109	2
Klenk	Blackthorn flower, ru...	N101109	2
Klenk	Blackthorn flower, ru...	1150n101109	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Kräuter Schulte	Blackthorn flower, ru...	53233	2
an	Blessed thistle, cut	13389704	1
Anzag	Blessed thistle, cut	282281	1
Bombastus	Blessed thistle, cut	271946	1
Caelo	Blessed thistle, cut	9355208	1
Caelo	Blessed thistle, cut	27111205	1
Caelo	Blessed thistle, cut	4743554	1
Caelo	Blessed thistle, cut	13025901	5
Caelo	Blessed thistle, cut	13025902	1
Caelo	Blessed thistle, cut	12038202	1
Caelo	Blessed thistle, cut	3091301	1
Caelo	Blessed thistle, cut	13025903	3
Caelo	Blessed thistle, cut	10325402	5
Caelo	Blessed thistle, cut	12038203	2
Caelo	Blessed thistle, cut	10325404	1
Caelo	Blessed thistle, cut	13389701	1
Gehe / 08.03.13 Redwood	Blessed thistle, cut	205007	1
Klenk	Blessed thistle, cut	A110517	1
Apofit	Blue bottle flower wi...	278776	1
Bombastus	Blue bottle flower wi...	275759	2
Bombastus	Blue bottle flower wi...	284030	1
Caelo	Blue bottle flower wi...	11059209	2
Caelo	Blue bottle flower wi...	12060203	4
Caelo	Blue bottle flower wi...	12232501	2
Caelo	Blue bottle flower wi...	12060202	2
Caelo	Blue bottle flower wi...	14323302	1
Caelo	Blue bottle flower wi...	15206601	1
Caelo	Blue bottle flower wi...	12060205	4
Caelo	Blue bottle flower wi...	11059206	2
Caelo	Blue bottle flower wi...	11059211	2
Galke	Blue bottle flower wi...	23131	2
Klenk	Blue bottle flower wi...		1
Caelo	Bogbean leaf, cut	12226101	1
Caelo	Bogbean leaf, cut	1226101	1
Caelo	Bogbean leaf, cut	13123901	2
Caelo	Bogbean leaf, cut	13123902	2
Caelo	Bogbean leaf, cut	12226104	1
Caesar/Noweda	Bogbean leaf, cut	1510U-01517	1
Caelo	Bogbean leaf, cut	13149001	1
Caelo	Boldo leaf, cut	11016509	1
Caelo	Boldo leaf, cut	655456	1
Caelo	Boldo leaf, cut	11016511	1
Caelo	Boldo leaf, cut	12064303	1
Caelo	Boldo leaf, cut	12227005	1
Caelo	Boldo leaf, cut	12064305	1
Caelo	Boldo leaf, cut	12064306	1
Caelo	Boldo leaf, cut	12227004	1
Galke	Boldo leaf, cut	19855	1
Klenk	Boldo leaf, cut	1911B090709	1
Klenk	Boldo leaf, cut	1911A100714	7
VDL	Boldo leaf, cut	11016503	1
Caelo	Bucho leaf	13056601	2
Caelo	Bucho leaf	13056602	2
Caelo	Bucho leaf	13056605	1
Kräuter Schulte	Bucho leaf	54519	1
Caelo	Buckwheat herb, cut	11212612	1
Caelo	Buckwheat herb, cut	11212808	2
Caelo	Buckwheat herb, cut	30041301	1
Caelo	Buckwheat herb, cut	2051303	1
Caelo	Buckwheat herb, cut	13051303	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Buckwheat herb, cut	11212809	1
Caelo	Buckwheat herb, cut	11212817	6
Caelo	Buckwheat herb, cut	11212807	2
Caelo	Buckwheat herb, cut	5111302	1
Caelo	Buckwheat herb, cut	11212810	1
Caelo	Buckwheat herb, cut	11212814	2
Caelo	Buckwheat herb, cut	13193203	1
Hepart AG	Buckwheat herb, cut	B120509	2
Klenk	Buckwheat herb, cut	4581B120509	3
Caelo	Buckwheat herb, cut	11212812	1
-	Burdock root, cut	5110I-02131	1
Caelo	Burdock root, cut	12295808	2
Caelo	Burdock root, cut	12295801	2
Caelo	Burdock root, cut	1100801	1
Caelo	Burdock root, cut	10073213	1
Caelo	Burdock root, cut	11100801	2
Caelo	Burdock root, cut	12295805	3
Caelo	Burdock root, cut	12295807	1
Caelo	Burdock root, cut	13122802	1
Caelo	Burdock root, cut	13122801	2
Caelo	Burdock root, cut	12295802	4
Caelo	Burdock root, cut	107063	1
Euro OTC	Burdock root, cut	13122803	1
Galke	Burdock root, cut	19802	1
Klenk	Burdock root, cut	6161A101206	1
Klenk	Burdock root, cut	6161A120208	4
Klenk	Burdock root, cut	A120206	1
Klenk	Burdock root, cut	A130214	1
Klenk	Burdock root, cut	6161A080709	1
Klenk	Burdock root, cut	6161A-101206	1
Klenk	Burdock root, cut	6161A120103	1
Klenk	Burdock root, cut	6161A-120103	1
Caelo	Burnet root	8111203	1
Caelo	Burnet root	12027411	3
Caelo	Burnet root	12027405	2
Caelo	Burnet root	12027403	1
Caelo	Burnet root	12027413	1
Caelo	Burnet root	12027409	1
Caelo	Burnet root	12027410	3
Fagron	Caffeine citrate	12C16-N03	1
Caelo	Caffeine citrate	11F21-N05	1
Caelo	Caffeine citrate	13D30-N02	9
Fagron	Caffeine citrate	10c23-n02	1
Fagron	Caffeine citrate	10H02-N02	2
Fagron	Caffeine citrate	2002311282	1
Fagron	Caffeine citrate	12J05-N06	1
Fagron	Caffeine citrate	204311282	1
Fagron	Caffeine citrate	2813E1282	1
Fagron	Caffeine citrate	13D30-No2	1
Fagron	Caffeine citrate	26021401	1
Fagron	Caffeine citrate	CCC1205	1
Fagron	Caffeine citrate	13D30-N02	1
Fagron	Caffeine citrate	11C29-N04	1
Fagron	Caffeine citrate	CCD-1401	3
Fagron	Caffeine citrate	15A05-B03	1
Fagron	Caffeine citrate	15A05B03	1
Fagron	Caffeine citrate	11082015A	1
Fagron	Caffeine citrate	15A05-B03-307135	3
Fagron	Caffeine citrate	15a05-b03-302746	1
Fagron	Caffeine citrate	13B08N02	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Caffeine citrate	15A05-B03-318006	13
Fagron	Caffeine citrate	2714E-01282	1
Fagron	Caffeine citrate	15A05-B03	3
Fagron	Caffeine citrate	15a05-b03-318006	1
Fagron	Caffeine citrate	11C29-N04	1
Fagron	Caffeine citrate	3513I-01282	1
Fagron	Caffeine citrate	4213U01282	1
Fagron	Caffeine citrate	5013U01282	1
Fagron	Caffeine citrate	3314E-01282	1
Fagron	Caffeine citrate	3914U-01282	1
Fargon	Caffeine citrate	12J05-N06	4
Fargon/Phoenix	Caffeine citrate	15A05-B03-302746	12
Fgron	Caffeine citrate	2013Q-01282	1
Gehe	Caffeine citrate	13B08-N02	3
Noweda	Caffeine citrate	CCC-1101	1
Rondell Apotheke	Caffeine citrate	15A05-B03-307309	2
Caelo	Calcium chloride dihy...	12341409	1
Caelo	Calcium chloride dihy...	11230921	2
Caelo	Calcium chloride dihy...	12341404	2
Caelo	Calcium chloride dihy...	11230915	1
Caelo	Calcium chloride dihy...	12341406	1
Caelo	Calcium chloride dihy...	12B09-N11	1
EUro/AHD	Calcium chloride dihy...	1205014-02	2
Caelo	Calcium chloride dihy...	8237314	1
Caelo	Calcium hydrogen phos...	10135223	1
Caelo	Calcium hydrogen phos...	11287503	2
Caelo	Calcium hydrogen phos...	10135228	1
Caelo	Calcium hydrogen phos...	11287510	1
Caelo	Calcium hydrogen phos...	101352009	1
Caelo	Calcium hydrogen phos...	12212804	5
Caelo	Calcium hydrogen phos...	12212806	1
Caelo	Calcium hydrogen phos...	12212812	2
Caelo	Calcium hydrogen phos...	12212811	5
Caelo	Calcium hydrogen phos...	14011401	1
Caelo	Calcium hydrogen phos...	14085301	1
Caelo	Calcium hydrogen phos...	13170701	6
Caelo	Calcium hydrogen phos...	12212816	1
Caelo	Calcium hydrogen phos...	12212813	1
Caelo	Calcium hydrogen phos...	11287501	1
Caelo	Calcium hydrogen phos...	11287509	2
Caelo	Calcium hydrogen phos...	10135201	1
Caelo	Calcium hydrogen phos...	12212822	1
Caelo	Calcium hydrogen phos...	13170704	2
Caelo	Calcium hydrogen phos...	10135216	1
Caelo	Calcium hydrogen phos...	12212807	1
Fagron	Calcium hydroxide	12J18-N01	1
Fagron	Calcium hydroxide	13D26-N14	1
Gehe	Calcium hydroxide	12F08-N02	3
Caelo	Calcium sulfate dihyd...	10132403	1
Caelo	Calcium sulfate dihyd...	12316301	1
Caelo	Calcium sulfate hemih...	14101701	1
Caelo	Calcium sulfate hemih...	9246320	1
Bombastus	Calendula flower	268626	1
Caelo	Calendula flower	12221706	2
Caelo	Calendula flower	13235503	3
Caelo	Calendula flower	15291501	1
Caelo	Calendula flower	12221710	1
Caelo	Calendula flower	12221705	1
Caelo	Calendula flower	12221511	1
Caelo	Calendula flower	12221508	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Calendula flower	122221707	1
Caelo	Calendula flower	12221708	3
Caelo	Calendula flower	12221510-3356319071	1
Caelo	Calendula flower	12221510-3435311151	1
Caelo	Calendula flower	13235502	3
galke,	Calendula flower	12028	1
Bombastus	Calendula flower	280306	1
Klenk	Calendula flower	1250A110511	1
Klenk	Calendula flower	C120321	1
Klenk	Calendula flower	1241B120312	1
Klenk	Calendula flower	1241B130517	1
Wolf	Calendula flower	23342	1
Anzag	Calendula flower, cut	12221706	12
Bahnhof-Apotheke	Calendula flower, cut	17-121106	1
Bombastus	Calendula flower, cut	270046	1
Bombastus	Calendula flower, cut	253620	1
Bombastus	Calendula flower, cut	279632	1
Bombastus	Calendula flower, cut	275813	1
Bombastus	Calendula flower, cut	275128	1
Bombastus	Calendula flower, cut	207294	1
Bombastus	Calendula flower, cut	234997	1
Caelo	Calendula flower, cut	13235502	9
Caelo	Calendula flower, cut	295556	1
Caelo	Calendula flower, cut	22061203	1
Caelo	Calendula flower, cut	12071201	1
Caelo	Calendula flower, cut	11187612	12
Caelo	Calendula flower, cut	11187610	3
Caelo	Calendula flower, cut	27101201	1
Caelo	Calendula flower, cut	19111206	1
Caelo	Calendula flower, cut	11187611	3
Caelo	Calendula flower, cut	31121202	1
Caelo	Calendula flower, cut	5021305	1
Caelo	Calendula flower, cut	12221705	4
Caelo	Calendula flower, cut	11221407	1
Caelo	Calendula flower, cut	12221704	11
Caelo	Calendula flower, cut	8041302	1
Caelo	Calendula flower, cut	3061301	1
Caelo	Calendula flower, cut	12221707	2
Caelo	Calendula flower, cut	21091301	1
Caelo	Calendula flower, cut	12221710	2
Caelo	Calendula flower, cut	9112013C	1
Caelo	Calendula flower, cut	13235501	4
Caelo	Calendula flower, cut	9121303	1
Caelo	Calendula flower, cut	18121301	1
Caelo	Calendula flower, cut	13235505	1
Caelo	Calendula flower, cut	13410202	2
Caelo	Calendula flower, cut	15040301	1
Caelo	Calendula flower, cut	10291904	1
Caelo	Calendula flower, cut	12221701	1
Caelo	Calendula flower, cut	122221704	1
Caelo	Calendula flower, cut	1187612	2
Caelo	Calendula flower, cut	12221708	11
Caelo	Calendula flower, cut	13235506	2
Caelo	Calendula flower, cut	AKD1	1
Caelo	Calendula flower, cut	1325502	1
Gehe	Calendula flower, cut	260205	1
Klenk	Calendula flower, cut	1241B130517	6
Klenk	Calendula flower, cut	1241B150902	1
Klenk	Calendula flower, cut	1241N151209	1
Klenk	Calendula flower, cut	1241B160530	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Calendula flower, cut	1241B120419	2
Klenk	Calendula flower, cut	112211448	1
Klenk	Calendula flower, cut	1240A110418	1
Klenk	Calendula flower, cut	204311448	1
Klenk	Calendula flower, cut	1241B130321	5
Klenk	Calendula flower, cut	3013E1448	1
Klenk	Calendula flower, cut	B130517	2
Klenk	Calendula flower, cut	1241B140211	1
Klenk	Calendula flower, cut	1241B130927	1
Klenk	Calendula flower, cut	1241B110118	2
Noweda	Calendula flower, cut	12221709	9
Klenk	Calendula flower, cut	1241C120321	4
Fagron	Calendula flower, cut	1241B120312	4
Sanacorp	Calendula flower, cut	12221601	4
Caelo	Calendula flower, cut	12221502	2
AHD	Camphor	17288306	9
Euro OTC	Camphor	1210030-02	1
an	Camphor	12344909	1
Caelo	Camphor	13205502	1
Caelo	Camphor	13195316	6
Caelo	Camphor		1
Caelo	Camphor	17288307	1
Caelo	Camphor	11286905	2
Caelo	Camphor	3091203	1
Caelo	Camphor	11032023	1
Caelo	Camphor	11074509	1
Caelo	Camphor	12054107	4
Caelo	Camphor	120564113	1
Caelo	Camphor	12054141	3
Caelo	Camphor	12344905	2
Caelo	Camphor	12054142	6
Caelo	Camphor	11286910	1
Caelo	Camphor	4101303	1
Caelo	Camphor	12054114	2
Caelo	Camphor	12243701	1
Caelo	Camphor	13205512	2
Caelo	Camphor	13205511	1
Caelo	Camphor	13195311	1
Caelo	Camphor	25041401	1
Caelo	Camphor	13195314	5
Caelo	Camphor	12061411	1
Caelo	Camphor	13195316	1
Caelo	Camphor	13205522	1
Caelo	Camphor	13205522	2
Caelo	Camphor	13195318	1
Caelo	Camphor	13K28-04-294937	1
Caelo	Camphor	13195322	7
Caelo	Camphor	4031503	1
Caelo	Camphor	13195327	1
Caelo	Camphor	13195326	3
Caelo	Camphor	14202807	3
Caelo	Camphor	15097803	2
Caelo	Camphor	15120901	2
Caelo	Camphor	14310705	1
Caelo	Camphor	15316807	7
Caelo	Camphor	15320604	5
Caelo	Camphor	1410710	1
Caelo	Camphor	14310713	9
Caelo	Camphor	15316819	6
Caelo	Camphor	150622C	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Camphor	140918C	1
Caelo	Camphor	15120902	1
Caelo	Camphor	16209304	3
Caelo	Camphor	14310710	2
Caelo	Camphor	14310718	5
Caelo	Camphor	15384201	1
Caelo	Camphor	15397701	1
Caelo	Camphor	16209305	8
Caelo	Camphor	16235405	2
Caelo	Camphor	14310722	3
Caelo	Camphor	16235404	3
Caelo	Camphor	16209306	1
Caelo	Camphor	15/18.B11-321658	1
Caelo	Camphor	162093029	1
Caelo	Camphor	17004304	1
Caelo	Camphor	17004302	3
Caelo	Camphor	17050605	19
Caelo	Camphor	13111707	1
Caelo	Camphor	13111708	1
Caelo	Camphor	1531607	1
Caelo	Camphor	17134703	2
Caelo	Camphor	17288301	5
Caelo	Camphor	17324104	4
Caelo	Camphor	7061802	1
Caelo	Camphor	7071801	1
Caelo	Camphor	17288305	1
Caelo	Camphor	12091805	1
Caelo	Camphor	12091808	1
Caelo	Camphor	18019806	15
Caelo	Camphor	18108904	5
Caelo	Camphor	6021901	1
Caelo	Camphor	15086806	1
Caelo	Camphor	16209301	11
Caelo	Camphor	13195301	1
Caelo	Camphor	13195301	2
Caelo	Camphor	13195304	1
Caelo	Camphor	13195311	1
Caelo	Camphor	16209309	14
Caelo	Camphor	12054149	9
Caelo	Camphor	444A170221	1
Caelo	Camphor	13195318	1
Caelo	Camphor	12228206	1
Caelo	Camphor	62(17288306)	1
Caelo	Camphor	3273	1
Caelo	Camphor	14310706	1
Caelo	Camphor	15316823	2
Caelo	Camphor	17050606	3
Caelo	Camphor	12054151	2
Caelo	Camphor	13195323	1
Caelo	Camphor	15316805	1
Caelo	Camphor	14224304	1
Caelo	Camphor	11286909	2
Caelo	Camphor	2344905	1
Caelo	Camphor	713A-01221	1
Caelo	Camphor	914E-01221	1
Caelo	Camphor	315E-01221	1
Caelo	Camphor	5315I-01221	1
Caelo	Camphor	14310715	1
Caelo	Camphor	14224303	3
Caelo	Camphor	1412023-01	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Camphor	18198003	1
Caelo	Camphor	18019811	4
Caelo	Camphor	12228205	1
Caelo	Camphor	12054124	2
Caelo	Camphor	12054143	1
Caelo	Camphor	2811Q-01221	1
Caelo	Camphor	13205512	1
Caelo	Camphor	15086801	1
Caelo	Camphor	15316806	2
Caelo	Camphor	15062701	1
Caelo	Camphor	15316815	4
Caelo	Camphor	16209310	1
Fagron	Camphor	18066404	4
Caelo	Camphor	13108106	2
Caelo	Camphor	13205501	2
Caelo	Camphor	17004308	1
Caelo	Camphor	14310705	13
Caelo	Camphor	14310703	1
Caelo	Camphor	13205511	2
Caelo	Camphor	2803020-01	1
Caelo	Camphor	14310709	5
Caelo	Camphor	4444A150721	1
Caelo	Camphor	13205517	1
Caelo	Camphor	14310109	1
Caelo	Camphor	15397704	5
Caelo	Camphor	17004301	16
Caelo	Camphor	18327905	1
Caelo	Camphor	12054105	1
Caelo	Camphor	13195314	3
Caelo	Camphor	13108118	2
Caelo	Camphor	14G23-B04-301879	2
Caelo	Camphor	15062702	3
Caelo	Camphor	15316801	4
Caelo	Camphor	15316812	1
Caelo	Camphor	16235407	1
Caelo	Camphor	16235402	1
Caelo	Camphor	14310702	1
Caesar & Loretz GmbH,...	Camphor	11032035	4
Caesar Loretz	Camphor	18327903	3
Caesar&Loretz	Camphor	14310719	1
Caesar/Noweda	Camphor	1032	1
Caesar/Noweda	Camphor	13195328	1
Calo/AHD	Camphor	15086803	1
Camphor & Allied Prod...	Camphor	16209302	1
Cealo/ Noweda	Camphor	13108116	1
EuRho	Camphor	2111E-01219	1
Euro OTC	Camphor	1210030-02	4
Euro OTC	Camphor	1202021	1
Euro OTC	Camphor	113Q-01221	1
Euro OTC	Camphor	121003001	1
Euro OTC	Camphor	130313-02	1
Euro OTC	Camphor	1309019-03	1
Euro OTC	Camphor	1210030-01	7
Euro OTC	Camphor	1101029-02/Ch241011	1
Euro OTC	Camphor	1210030-01	1
Euro OTC	Camphor	1406029-02	2
Euro OTC	Camphor	121003002	1
Euro OTC	Camphor	1202021-02	2
Euro OTC	Camphor	1406029-01	2
Euro OTC	Camphor	1101029-02	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Euro OTC	Camphor	1303013-02	11
euro/ Sanacorp	Camphor	17050602	2
Euro OTC	Camphor	821509	1
Euro OTC	Camphor	1309019-02	1
Euro OTC	Camphor	2803020-01	1
Euro OTC	Camphor	1303013-01	5
Fagron	Camphor	12G02-N09	1
Fagron	Camphor	12D23-N03	1
Fagron	Camphor	11K23-N04	1
Fagron	Camphor	690442	1
Fagron	Camphor	13H23-B40-291888	1
Fagron	Camphor	13H23-B40-294116	1
Fagron	Camphor	8082014A	1
Fagron	Camphor	13h23-b40-294116	1
Fagron	Camphor	14G23-B04-296868	1
Fagron	Camphor	1309019-02	1
Fagron	Camphor	13K28-B04-289340	1
Fagron	Camphor	15/18-B11-321658	1
Fagron	Camphor	17L01-B03	1
Fagron	Camphor	13H23-B04-288376	1
Fagron	Camphor	13K28-B04-294937	1
Fagron	Camphor	14G23-B04-301878	2
Fagron	Camphor	14G23-B04-299202	2
Fagron	Camphor	27011	1
Fagron	Camphor	825653	1
Fagron	Camphor	14G23-B04	2
Fagron	Camphor	13K28-B04	1
Fagron	Camphor	13H23-B40-296252	1
Fagron	Camphor	11H30-N15	1
Fagron	Camphor	13K28-B04	2
Fagron	Camphor	13K28_B04_294933	1
Fagron	Camphor	15097801	1
Fagron	Camphor	12B14-N09	1
Galke	Camphor	23624	1
Gatt-Koller	Camphor	1800202	3
Gehe	Camphor	17134702	3
GEHE	Camphor	16235408	2
Caelo	Camphor	14224303	1
Caelo	Camphor	17050605/1140418	1
Klenk	Camphor	444A160817	6
Klenk	Camphor	444A150721	1
Klenk	Camphor	444A100826	1
Klenk	Camphor	444A180815	3
Klenk	Camphor	444A170224	3
Klenk	Camphor	444A150721	1
Klenk	Camphor	444A140526	5
L12	Camphor	18108901	1
Caelo	Camphor	15397705	1
Nachprüfung	Camphor	1616E-01221	1
Nachtestung-Verlänger...	Camphor	242/17	1
Noweda	Camphor	1202021-01	3
Caelo	Camphor	14202801	3
Phoenix	Camphor	15316811	7
Phoenix	Camphor	160209309	1
Phoenix	Camphor	3382	1
Caelo	Camphor	12054113	1
phönix	Camphor	444a160817	1
Phönix	Camphor	18019803	10
Post-Apotheke 22.01.2...	Camphor	11032012	1
Sanacorp	Camphor	444A130115	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Sanacorp	Camphor	14310720	2
Sanacorp	Camphor	17004306	10
Sanacorp	Camphor	18019802	8
Caelo	Camphor	15097802	2
Caelo	Camphor	18108902	1
Caelo	Camphor	18108905	2
xxx	Camphor	709E-01221	1
Alfred Galke	Caraway fruit	20069	1
Anzag ek: 2,59EUR 19.09...	Caraway fruit	11003216	3
Caelo	Caraway fruit	12226609	5
Bahnhof-Apotheke	Caraway fruit	18-120709	1
Bombastus	Caraway fruit	275849	1
Bombastus	Caraway fruit	282269	1
Bombastus	Caraway fruit	270124	1
Caelo	Caraway fruit	12226603	7
Caelo	Caraway fruit	12226606	2
Caelo	Caraway fruit	12226504	1
Caelo	Caraway fruit	11003207	1
Caelo	Caraway fruit	27121202	1
Caelo	Caraway fruit	12343403	1
Caelo	Caraway fruit	11003211	1
Caelo	Caraway fruit	2103311537	1
Caelo	Caraway fruit	12226601	1
Caelo	Caraway fruit	4061303	1
Caelo	Caraway fruit	11378309	1
Caelo	Caraway fruit	413M	1
Caelo	Caraway fruit	12226614	2
Caelo	Caraway fruit	12226608	1
Caelo	Caraway fruit	13306003	1
Caelo	Caraway fruit	13397102	2
Caelo	Caraway fruit	13397104	2
Caelo	Caraway fruit	13091401	1
Caelo	Caraway fruit	13306004	1
Caelo	Caraway fruit	13306005	2
Caelo	Caraway fruit	13306006	4
Caelo	Caraway fruit	13306008	1
Caelo	Caraway fruit	15097109	1
Caelo	Caraway fruit	15409103	2
Caelo	Caraway fruit	16308502	1
Caelo	Caraway fruit	16165308	1
Caelo	Caraway fruit	15409105	1
Caelo	Caraway fruit	15409104	2
Caelo	Caraway fruit	15409102	1
Caelo	Caraway fruit	11121704	1
Caelo	Caraway fruit	18121717	1
Caelo	Caraway fruit	16308504	1
Caelo	Caraway fruit	11003217	5
Caelo	Caraway fruit	12226611	3
Caelo	Caraway fruit	15097101	8
Caelo	Caraway fruit	1509101	1
Caelo	Caraway fruit	16308503	2
Caelo	Caraway fruit	13397105	8
Caelo	Caraway fruit	15097103	3
Caelo	Caraway fruit	290416	1
Caelo	Caraway fruit	15097115	6
Caelo	Caraway fruit	15409101	1
Caelo	Caraway fruit	12226501	5
Caelo	Caraway fruit	9267815	1
Caelo	Caraway fruit	811E-01537	1
Caelo	Caraway fruit	17256303	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Caraway fruit	15097111	1
Caelo	Caraway fruit	15097116	1
Caelo	Caraway fruit	13306002	5
Caelo	Caraway fruit	15097108	4
Caelo	Caraway fruit	16308501	1
Caelo	Caraway fruit	12226612	8
Caelo	Caraway fruit	15097107	2
Caesar & Loretz GmbH,...	Caraway fruit	9267824	2
Caesar & Loretz GmbH,...	Caraway fruit	11003213	2
Caesar & Loretz/Noweda	Caraway fruit	15056601	1
Galke	Caraway fruit	21257	1
Galke	Caraway fruit	23627	1
Galke	Caraway fruit	27450	1
GALKE	Caraway fruit	30030	1
Klenk	Caraway fruit	2770A130910	1
Hepart AG	Caraway fruit	B-224, kBA	1
Caelo	Caraway fruit	12226608	4
Caelo	Caraway fruit	1222608	1
Klenk	Caraway fruit	2770A110601	9
Klenk	Caraway fruit	2770A110818	8
Klenk	Caraway fruit	1810A-01537	1
Klenk	Caraway fruit	A120905	3
Klenk	Caraway fruit	2770A130521	12
Klenk	Caraway fruit	2270A130521	1
Klenk	Caraway fruit	412091-1-P	1
Klenk	Caraway fruit	2770A131008	2
Klenk	Caraway fruit	2820A150713	1
Klenk	Caraway fruit	2770A120403	14
Klenk	Caraway fruit	2770a120905	2
Klenk	Caraway fruit	5213A1537	1
Klenk	Caraway fruit	2770A140708	6
Klenk	Caraway fruit	2770A160304	2
Noweda	Caraway fruit	12226503	7
Noweda	Caraway fruit	12226605	3
Caelo	Caraway fruit	13041903	1
Caelo	Caraway fruit	2041017/16308501	1
sanacorp	Caraway fruit	2656259	1
Sanacorp	Caraway fruit	2770A120905	4
Sanacorp	Caraway fruit		2
Caelo	Caraway fruit	12226604	5
Caelo	Caraway fruit	13041901	1
VDL;15.06.15;6,83EUR	Caraway fruit	13306007	1
Wolf	Caraway fruit	B-224	1
Caelo	Caraway fruit, pounded	12116904	3
Caelo	Caraway fruit, pounded	13367101	1
Galke	Caraway fruit, pounded	18943	1
Apomix / 11	Carbachol	12330703	1
Caelo	Cardamom fruit	11309110	1
Caelo	Cardamom fruit	13260502-3537411072	1
Klenk	Cardamom fruit	2750A110810	2
Klenk	Cardamom fruit	A110810	3
Klenk	Cardamom fruit	A130807	1
Caelo	Cardamom fruit	13026003	1
Caelo	Cayenne pepper, powde...	13205106	1
Caelo	Celery root, cut	12319105	2
Caelo	Celery root, cut	12319107	1
Caelo	Celery root, cut	10270009	1
Caelo	Celery root, cut	10270012	1
Caelo	Celery root, cut	12319108	1
Bombastus	Centaury, cut	277598	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Aurica/Phönix	Centaury, cut	520702152	1
Caelo	Centaury, cut	12268608	10
Caelo	Centaury, cut	11097605	2
Caelo	Centaury, cut	11097609	3
Caelo	Centaury, cut	10104012	1
Caelo	Centaury, cut	8021302	1
Caelo	Centaury, cut	15224102	1
Caelo	Centaury, cut	12268606	14
Caelo	Centaury, cut	12379601	1
Caelo	Centaury, cut	11097602	1
Caelo	Centaury, cut	3711B120628	1
Caelo	Centaury, cut	12268601	3
Caelo	Centaury, cut	12268605	4
Caelo	Centaury, cut	12268602	19
Finze	Centaury, cut	11097610	1
Galke	Centaury, cut	9721	1
Klenk	Centaury, cut	3711B111216	1
Klenk	Centaury, cut	B120628	1
Klenk	Centaury, cut	3711B-111216	1
Phoenix	Centaury, cut	11097612	9
Phönix	Centaury, cut	11093612	2
Klenk	Ceylon cinnamon, fine...	614B160818	1
Klenk	Ceylon cinnamon, fine...	614B120411	2
Klenk	Ceylon cinnamon, fine...	611B100628	1
Klenk	Ceylon cinnamon, fine...	614B121010	2
Klenk	Ceylon cinnamon, fine...	614b121024	1
Klenk	Ceylon cinnamon, fine...	614a120411	1
Klenk	Ceylon cinnamon, fine...	615B130325	3
Klenk	Ceylon cinnamon, fine...	614B121024	4
Caelo	Ceylonese Cinnamon, p...	12242806	2
Caelo	Ceylonese Cinnamon, p...	12242815	1
Caelo	Ceylonese Cinnamon, p...	12242818	1
Klenk	Ceylonese Cinnamon, p...	614B151008	1
Klenk	Ceylonese Cinnamon, p...	614B161128	1
-	Chelidonium majus her...	810I-01632	1
Klenk	Chelidonium majus her...	1406111632	1
Caelo	Chelidonium majus her...	311092	1
Galke	Chelidonium majus her...	20937	3
Klenk	Chelidonium majus her...	3731A110301	6
Klenk	Chelidonium majus her...	3731A120611	4
Klenk	Chelidonium majus her...	4711E-01632	1
Klenk	Chelidonium majus her...	3731A130904	5
Klenk	Chelidonium majus her...	3731B100205	1
Klenk	Chelidonium majus her...	3731K120904	4
-	Chickweed, cut	2011A-01686	1
Caelo	Chickweed, cut	13040501	1
Caelo	Chickweed, cut	13040503	1
Caelo	Chickweed, cut	13254403	2
Caelo	Chickweed, cut	13254401	1
Caelo	Chickweed, cut	4551B130902	1
Caelo	Chickweed, cut	14212411	1
Caelo	Chickweed, cut	16143608	1
Caelo	Chickweed, cut	13040502-3283310662	1
Caelo	Chickweed, cut	13040502	2
Caelo	Chickweed, cut	13254404	1
Caelo	Chickweed, cut	13040504	1
Klenk	Chickweed, cut	4551b110222	1
Klenk	Chickweed, cut	4551B090528	1
Phoenix	Chickweed, cut	18100704	1
Caelo	Chickweed, cut	14212405	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
-	Chicory herb, cut	4411I-01634	1
Caelo	Chicory herb, cut	12034302	1
Caelo	Chicory herb, cut	12034303	3
Caelo	Chicory herb, cut	12354302	3
Caelo	Chicory herb, cut	14031315	1
Caelo	Chicory herb, cut	12354304	1
Caelo	Chicory herb, cut	12354306	1
Caelo	Chicory herb, cut	12369102	3
Caelo	Chicory herb, cut	12034301	2
Klenk	Chicory herb, cut	3751A120123	2
Klenk	Chicory herb, cut	A120123	2
Klenk	Chicory herb, cut	3751A080902	1
Klenk	Chicory herb, cut	3751A120307	7
Klenk	Chicory herb, cut	3751a120307	1
Klenk	Chicory herb, cut	3751c120614	1
Klenk	Chicory herb, cut	3751A-100118	1
Klenk	Chicory herb, cut	4510I-01634	1
Sanacorp	Chicory herb, cut	12369101	6
Klenk	Chicory root, cut	66221A101202	1
Caelo	Chicory root, cut	6221A101202	4
Caelo	Chicory root, cut	11374501	1
Caelo	Chicory root, cut	11374504	3
Caelo	Chicory root, cut	11374506	1
Caelo	Chicory root, cut	6221As101202	1
Caelo	Chicory root, cut	11081803	1
Caelo	Chicory root, cut	11374510	2
Caelo	Chicory root, cut	91338319	1
Klenk	Chicory root, cut	6221A090311	1
Klenk	Chicory root, cut	6221N130201	1
Klenk	Chicory root, cut	A130304	1
Klenk	Chicory root, cut	6221A130304	1
Kräuter Schulte	China Pai Mu Tan	52783	1
Fagron	Chlorhexidine dihydro...	14A09B03	1
Fagron	Chlorhexidine dihydro...	14A09-B03-293425	1
Euro OTC	Cholecalciferol dry c...	1012025-01	1
Euro OTC	Cholecalciferol dry c...	1508032-01	2
Euro OTC	Cholecalciferol dry c...	1701053-01	11
Euro OTC	Cholecalciferol dry c...	150803201	1
Euro OTC	Cholecalciferol dry c...	1707027-01	17
Euro OTC	Cholecalciferol dry c...	1801038-01	4
Euro OTC	Cholecalciferol dry c...	1802014-01	17
Euro OTC	Cholecalciferol dry c...	170153-01	5
Euro OTC	Cholecalciferol dry c...	1806003-01	28
Euro OTC	Cholecalciferol dry c...	1502021-01	1
Euro OTC	Cholecalciferol dry c...	1210051-01	1
Euro OTC	Cholecalciferol dry c...	1602019-01	2
Euro OTC	Cholecalciferol dry c...	L1403012-01	1
Euro OTC	Chromium yeast 0.2%	L1311026-01	1
Fagron	Cinchocaine hydrochlo...	12F25-N10	1
Phönix	Cinchocaine hydrochlo...	13E13-N07	1
Caelo	Cinchona bark, cut	10381906	1
Caelo	Cinchona bark, cut	15301904	2
Caelo	Cinchona bark, cut	14009305	1
Klenk	Cinchona bark, cut	601B130415	1
Klenk	Cinchona bark, cut	601B130415	1
Caelo	Cinnamon rods (Ceylon...	12148904	1
Klenk	Cinnamon rods (Ceylon...	A101018	1
Klenk	Cinnamon rods (Ceylon...	B121016	1
Klenk	Cinnamon rods (Ceylon...	610A101018	1
Phönix	Cinnamon rods (Ceylon...	610A130927	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Sanacorp	Cinnamon rods (Ceylon...	13231601	1
Akazie	Cinnamon, cut	20.09.2015	1
Akazien-Apo	Cinnamon, cut	Test	1
Caelo	Cinnamon, cut	11357909	1
Caelo	Cinnamon, cut	11357912	2
Caelo	Cinnamon, cut	12309902	3
Caelo	Cinnamon, cut	12309908	1
Caelo	Cinnamon, cut	25111307	1
Caelo	Cinnamon, cut	12309909	1
Caelo	Cinnamon, cut	13304401	2
Caelo	Cinnamon, cut	13304415	1
Caelo	Cinnamon, cut	13304402	2
Caelo	Cinnamon, cut	13304409	1
Caelo	Cinnamon, cut	13304407	1
Caelo	Cinnamon, cut	15151905	1
Caelo	Cinnamon, cut	16061702	1
Fargon / Gehe	Cinnamon, cut	15104201	1
Caelo	Cinnamon, cut	15151902	1
Klenk	Cinnamon, cut	610A101018	1
Klenk	Cinnamon, cut	610A130927	1
siehe Protokoll	Cinnamon, cut	sieheProtokoll	1
Fargon	Cinnarizine	13H01-N07	4
Fargon	Cinnarizine	14D09-B01-292883	1
Fargon	Cinnarizine	14D09-B01	3
Fargon	Cinnarizine	8D11-N04	1
Fargon	Cinnarizine	13I26-N22	1
Fargon	Cinnarizine	13I26-N22	1
Caelo	Clindamycin-2-dihydro...	14257305	1
Caelo	Clindamycin-2-dihydro...	17344102	1
Caelo	Clindamycin-2-dihydro...	16326507	1
Caelo	Clindamycin-2-dihydro...	17344101	5
Caesar & Loretz GmbH	Clindamycin-2-dihydro...	19122401	1
Fargon	Clobetasol-17-propion...	12A03-N03	1
Fargon	Clobetasol-17-propion...	11k04-n17	1
Fargon	Clobetasol-17-propion...	12 19-N01	1
Fargon	Clobetasol-17-propion...	12I19-N01	1
Fargon	Clobetasol-17-propion...	12I19-N01	2
Fargon	Clobetasol-17-propion...	12K08-N02	2
Fargon	Clobetasol-17-propion...	13W16-N01	1
Fargon	Clobetasol-17-propion...	12L19-N06	1
Fargon	Clobetasol-17-propion...	12/19-No1	1
Fargon	Clobetasol-17-propion...	12/19-N01003637	1
Caelo	Clove	5398872	1
Caelo	Clove	12095802	1
Caelo	Clove	11233305	1
Caelo	Clove	12095807	5
Caelo	Clove	12095806	2
Caelo	Clove	12266505	1
Caelo	Clove	13371309	1
Caelo	Clove	14057602	1
Klenk	Clove	1260A110608	5
Klenk	Clove	1260A100617	2
Klenk	Clove	1260A101223	1
Klenk	Clove	A120328	1
Klenk	Clove	1260A120328	6
Klenk	Clove	1260A130903	3
Klenk	Clove	1260A150304	2
Caelo	Clove, powdered (spice)	14180001	1
Caelo	Clove, powdered (spice)	12355303	1
Caelo	Cocaine hydrochloride	12329103	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Cocaine hydrochloride	13259306	1
Caelo	Cocaine hydrochloride	14069209	1
Caelo	Cocaine hydrochloride	17003902	2
Caelo	Cocaine hydrochloride	18266104	2
Caelo	Cocaine hydrochloride	18J01-B07-353630	2
Caelo	Cocaine hydrochloride	13112102	1
Fagron	Cocaine hydrochloride	12G23-N13	1
Fagron	Cocaine hydrochloride	13G03-N08	2
Fagron	Cocaine hydrochloride	14H27-B03	1
Fagron	Cocaine hydrochloride	15E12-B03	1
Fagron	Cocaine hydrochloride	16B11-B05-323385	1
Fagron	Cocaine hydrochloride	15-00638	1
Gatt-Koller	Cocaine hydrochloride	20172282	1
Macfarlan Smith/Noweda	Cocaine hydrochloride	15224802	2
Caelo	Cocaine hydrochloride	16051402	1
Synopharm	Cocaine hydrochloride	16B11-B05	1
Caelo	Cocoa bark, cut	19011303	1
Caelo	Cocoa bark, cut	12126901	1
Caelo	Cocoa bark, cut	12126907	1
Caelo	Cocoa bark, cut	12126910	1
Caelo	Cocoa bark, cut	12126905	2
Caelo	Cocoa bark, cut	1216907	1
Caelo	Codeine phosphate hem...	15350703	2
Caelo	Codeine phosphate hem...	17160503	3
Caelo	Codeine phosphate hem...	18187903	3
Caelo	Codeine phosphate hem...	18187960	2
Caelo	Codeine phosphate hem...	16169805	3
Caelo	Codeine phosphate hem...	14275910	1
Caelo	Codeine phosphate hem...	18187907	1
Caelo	Codeine phosphate hem...	15219805	2
Caelo	Codeine phosphate hem...	16349708	2
Caelo	Codeine phosphate hem...	1427910	1
Caelo	Codeine phosphate hem...	13I27-N06	1
Caelo	Codeine phosphate hem...	16349704	2
Caelo	Codeine phosphate hem...	16349707	1
Caelo	Codeine phosphate hem...	17L22-B03-343752	1
Caesar & Loretz GmbH	Codeine phosphate hem...	18187906	5
Caesar & Loretz GmbH	Codeine phosphate hem...	18187902	2
Caesar & Loretz GmbH	Codeine phosphate hem...	18187901	1
Euro OTC	Codeine phosphate hem...	CP04236	1
Euro/ Sanacorp	Codeine phosphate hem...	15F09-B02-315564	2
Fagron	Codeine phosphate hem...	11/19-N10	1
Fagron	Codeine phosphate hem...	12C05-N01	1
Fagron	Codeine phosphate hem...	13E21-N04	1
Fagron	Codeine phosphate hem...	13C11-N10	1
Fagron	Codeine phosphate hem...	1615I-01279	1
Fagron	Codeine phosphate hem...	13/27-N06	2
Fagron	Codeine phosphate hem...	15B17-B99-304623	1
Fagron	Codeine phosphate hem...	15F09-B02-310520	2
Fagron	Codeine phosphate hem...	15F09-B02	1
Fagron	Codeine phosphate hem...	15F09-B02-314033	1
Fagron	Codeine phosphate hem...	16E17-B05-324109	4
Fagron	Codeine phosphate hem...	913I-01279	1
Gehe	Codeine phosphate hem...	15350710	3
Merck	Codeine phosphate hem...	120765	1
Caelo	Codeine phosphate hem...	16349706	2
Caelo	Codeine phosphate hem...	130715	1
Th. Geyer	Codeine phosphate hem...	67038	1
Th. Geyer	Codeine phosphate hem...	67054	31
Fagron	Colophony	15186807	8

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Coltsfoot leaf, cut	277848	2
Bombastus	Coltsfoot leaf, cut	269501	3
Bombastus	Coltsfoot leaf, cut	272019	1
Bombastus	Coltsfoot leaf, cut	276303	5
Bombastus	Coltsfoot leaf, cut	285263	3
Bombastus	Coltsfoot leaf, cut	265856	1
Bombastus	Coltsfoot leaf, cut	274289	5
Bombastus	Coltsfoot leaf, cut	275489	3
Bombastus	Coltsfoot leaf, cut	281100	4
Bombastus	Coltsfoot leaf, cut	277131	1
Bombastus	Coltsfoot leaf, cut	232339	1
Bombastus	Coltsfoot leaf, cut	278758	7
Caelo	Coltsfoot leaf, cut	23041302	1
Caelo	Coltsfoot leaf, cut	Int.Ch:Now16081	1
Gehe	Coltsfoot leaf, cut	2021B121204	9
Klenk	Coltsfoot leaf, cut	8061207	1
Klenk	Coltsfoot leaf, cut	11101202	1
Klenk	Coltsfoot leaf, cut	2021B120124	4
Klenk	Coltsfoot leaf, cut	2021B120601	5
Klenk	Coltsfoot leaf, cut	5011301	1
Klenk	Coltsfoot leaf, cut	20021301	1
Klenk	Coltsfoot leaf, cut	KS100061	1
Klenk	Coltsfoot leaf, cut	2021B130319	4
Klenk	Coltsfoot leaf, cut	B120124	1
Klenk	Coltsfoot leaf, cut	26091301	1
Klenk	Coltsfoot leaf, cut	14111302	1
Klenk	Coltsfoot leaf, cut	5122013a	1
Klenk	Coltsfoot leaf, cut	23121302	1
Klenk	Coltsfoot leaf, cut	B130227	1
Klenk	Coltsfoot leaf, cut	2021C140730	1
Klenk	Coltsfoot leaf, cut	2021B150407	1
Klenk	Coltsfoot leaf, cut	2020B120124	1
Klenk	Coltsfoot leaf, cut	2021B130227	12
Klenk	Coltsfoot leaf, cut	2021B111005	1
Klenk	Coltsfoot leaf, cut	2021B140131	1
Klenk	Coltsfoot leaf, cut	2021b121204	1
Klenk	Coltsfoot leaf, cut	2021C130326	8
Noweda	Coltsfoot leaf, cut	2021B111111	3
Phönix	Coltsfoot leaf, cut	278296	4
Klenk	Coltsfoot leaf, cut	2021B121203	5
Bombastus	Comfrey herb, cut	281531	1
Klenk	Comfrey herb, cut	4561B100518	2
Caelo	Comfrey root	2711Q-02135	1
Caelo	Comfrey root	116053	1
Hof-Apotheke,St.Afra	Comfrey root	125041	1
Klenk	Comfrey root	6241B120531	3
Klenk	Comfrey root	6241B120807	4
Klenk	Comfrey root	6241B100715	1
Klenk	Comfrey root	6241B130619	8
Klenk	Comfrey root	B130619	1
Klenk	Comfrey root	6241B130724	7
Klenk	Comfrey root	6241B131009	1
Klenk	Comfrey root	6241B121214	2
Klenk	Comfrey root	6244B130624	1
Klenk	Comfrey root	6241B06110202	1
Klenk	Comfrey root	6241B130312	3
Klenk	Comfrey root	6241b130619	1
Klenk	Comfrey root	6241b130724	1
Klenk	Comfrey root	6241b120807	1
Caelo	Common broom herb, cut	11132209	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Common broom herb, cut	4412Q-01680	1
Caelo	Common broom herb, cut	12358802	1
Caelo	Common broom herb, cut	12358804	3
Caelo	Common broom herb, cut	12358805	1
Caelo	Common broom herb, cut	13241601	1
Galke	Common broom herb, cut	12358803	4
Phönix	Common broom herb, cut	12358801	2
Caelo	Common wormwood herb,...	12016708	5
Aurica	Common wormwood herb,...	521305386	1
Caelo	Common wormwood herb,...	12016702	1
Caelo	Common wormwood herb,...	3591A110119	4
Caelo	Common wormwood herb,...	12016705	5
Caelo	Common wormwood herb,...	12016707	3
Caelo	Common wormwood herb,...	18031302	1
Caelo	Common wormwood herb,...	1081301	1
Caelo	Common wormwood herb,...	12382702	12
Caelo	Common wormwood herb,...	12382705	2
Caelo	Common wormwood herb,...	12382706	1
Caelo	Common wormwood herb,...	14360605	1
Caelo	Common wormwood herb,...	12016709	2
Caelo	Common wormwood herb,...	12016711	3
Caelo	Common wormwood herb,...	12382701	7
Caelo	Common wormwood herb,...	9355403	1
Galke	Common wormwood herb,...	21637	1
Caelo	Common wormwood herb,...	10355329	1
Caelo	Common wormwood herb,...	1238701	1
Klenk	Common wormwood herb,...	3591A120123	8
Klenk	Common wormwood herb,...	A120123	2
Klenk	Common wormwood herb,...	3591A130218	10
Klenk	Common wormwood herb,...	3591a130218	2
Klenk	Common wormwood herb,...	3591a120123	1
Klenk	Common wormwood herb,...	2591A130218	1
Klenk	Common wormwood herb,...	3591A11119	1
Richter	Common wormwood herb,...	b200112	1
Caelo	Copper (II) sulfate p...	3411M-01317	1
Caelo	Copper (II) sulfate p...	12157107	1
Caelo	Copper (II) sulfate p...	10L15-N06	1
Caelo	Copper (II) sulfate p...	3211M-01317	1
Caelo	Copper (II) sulfate p...	2913U-01317	1
Fagron	Copper (II) sulfate p...	13A25-N06	1
Bombastus	Coriander	263733	1
Bombastus	Coriander	306310	1
Caelo	Coriander	13010304	1
Caelo	Coriander	12080901	2
Caelo	Coriander	14031316	1
Caelo	Coriander	13010302	2
Caelo	Coriander	27061305	1
Caelo	Coriander	4091305	1
Caelo	Coriander	13010306	2
Caelo	Coriander	16010209	1
Caelo	Coriander	12080906	1
Caelo	Coriander	9285707	1
Caelo	Coriander	16010201	1
Caesar/Noweda	Coriander	2010M-01539	1
Klenk	Coriander	2790A161111	5
Caelo	Coriander	12080905	1
Klenk	Coriander	2790A121023	7
Klenk	Coriander	A121023	3
Klenk	Coriander	2790A130129	2
Klenk	Coriander	2709A130129	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Coriander	2790A151117	1
Klenk	Coriander	2790a121023	1
Caelo	Coriander	18010209	1
sanacorp;3,32;18.06.15	Coriander	13299495	1
Caelo	Cottonwood bud	12027506	1
Caelo	Cottonwood bud	70864257	1
Klenk	Cottonwood bud	3260A120828	1
Caelo	Cottonwood bud	12027504	1
Bombastus	Couch grass rhizome, ...	276777	3
Bombastus	Couch grass rhizome, ...	273387	3
Bombastus	Couch grass rhizome, ...	270500	2
Bombastus	Couch grass rhizome, ...	278926	1
Bombastus	Couch grass rhizome, ...	262175	1
Caelo	Couch grass rhizome, ...	10049614	1
Caelo	Couch grass rhizome, ...	10049618	2
Caelo	Couch grass rhizome, ...	10349705	1
Caelo	Couch grass rhizome, ...	10349704	1
Caelo	Couch grass rhizome, ...	3712I-02180	1
Caelo	Couch grass rhizome, ...	12186817	3
Caelo	Couch grass rhizome, ...	12186705	1
Caesar/Noweda	Couch grass rhizome, ...	12186813	4
Galke	Couch grass rhizome, ...	18781	1
Gehe	Couch grass rhizome, ...	12186704	1
Gehe	Couch grass rhizome, ...	283061	1
Kräuter Schulte	Couch grass rhizome, ...	53016	2
Caelo	Cowberry leaf, cut	12105201	1
Caelo	Cowberry leaf, cut	12105203	1
Caelo	Cowberry leaf, cut	12150205	1
Caelo	Cowberry leaf, cut	11334302	1
Klenk	Cowberry leaf, cut	2431B101006	2
Creapure	Creatine	515941	1
Degussa / falcento	Creatine	422031	1
Phönix	Creatine	mysjhskeu	1
Euro OTC	Cysteine hydrochlorid...	1304019-01	1
Falcento	D-(+)-mannose	R-4638	1
Falcento	D-(+)-mannose	R-4639	1
Falcento	D-(+)-mannose	R4640	1
Falcento	D-(+)-mannose	R-4641	1
Giusto Faravelli	D-(+)-mannose	161004/1710215001	1
Caelo	Daisy flower	11103201	2
Caelo	Daisy flower	11068308	1
Caelo	Daisy flower	1210a120215	2
Caelo	Daisy flower	12133703	1
Caelo	Daisy flower	12133704	1
Caelo	Daisy flower	12133705	1
Caelo	Daisy flower	11103203	2
Hepart AG	Daisy flower	A130307	1
Kenk / Phoenix	Daisy flower	1210A130307	4
Klenk	Daisy flower	A130705	1
Klenk	Daisy flower	1210A110223	1
Klenk	Daisy flower	1210A120215	4
Klenk	Daisy flower	1210a071301	1
Klenk	Damiana leaf, cut	12064101	1
Caelo	Damiana leaf, cut	12330402	7
Caelo	Damiana leaf, cut	12330403	2
Caelo	Damiana leaf, cut	12330401	5
Caelo	Damiana leaf, cut	12064103	3
Caelo	Damiana leaf, cut	11026607	2
Caelo	Damiana leaf, cut	12330407	2
Klenk	Damiana leaf, cut	A130206	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Damiana leaf, cut	1990A130206	1
Noweda	Damiana leaf, cut	200151	1
Redwood	Damiana leaf, cut	216451	1
Anzag	Dandelion herb with r...	274030	1
Anzag 10.05.13 ek:3,16EUR	Dandelion herb with r...	6611B130321	1
Anzag 25.10.12 ek:3.16EUR	Dandelion herb with r...	6611B110131	1
Aurica	Dandelion herb with r...	521200197	1
Bombastus	Dandelion herb with r...	258809	1
Bombastus	Dandelion herb with r...	271272	5
Bombastus	Dandelion herb with r...	274030	5
Bombastus	Dandelion herb with r...	280363	5
Bombastus	Dandelion herb with r...	285264	1
Bombastus	Dandelion herb with r...	290125	1
Bombastus	Dandelion herb with r...	275126	1
Bombastus	Dandelion herb with r...	280363-3385310110	1
Bombastus	Dandelion herb with r...	282916	7
Caelo	Dandelion herb with r...	20111202	1
Caelo	Dandelion herb with r...	13108801	4
Caelo	Dandelion herb with r...	11030309	2
Caelo	Dandelion herb with r...	806212165	1
Caelo	Dandelion herb with r...	8111205	1
Caelo	Dandelion herb with r...	12236003	3
Caelo	Dandelion herb with r...	12236002	8
Caelo	Dandelion herb with r...	2112122165	1
Caelo	Dandelion herb with r...	11371903	1
Caelo	Dandelion herb with r...	11030305	1
Caelo	Dandelion herb with r...	13019802	19
Caelo	Dandelion herb with r...	13018902	1
Caelo	Dandelion herb with r...	Int.Ch:318090	1
Caelo	Dandelion herb with r...	13199202	2
Caelo	Dandelion herb with r...	17121305	1
Caelo	Dandelion herb with r...	13317903	1
Caelo	Dandelion herb with r...	Ch.-B.:13019802	1
Caelo	Dandelion herb with r...	11030313	2
Caelo	Dandelion herb with r...	12236001	3
Caelo	Dandelion herb with r...	6611B100902	1
Caelo	Dandelion herb with r...	13019805	1
Caelo	Dandelion herb with r...	13019802-3395310101	1
Caelo	Dandelion herb with r...	12236005	5
Caelo	Dandelion herb with r...	1103011	1
Caelo	Dandelion herb with r...	13019801	5
Caelo	Dandelion herb with r...	11030311	2
Caelo	Dandelion herb with r...	11030314	4
Caelo	Dandelion herb with r...	13108802	11
Caelo	Dandelion herb with r...	7341703	1
Euro OTC	Dandelion herb with r...	11030312	4
Galke	Dandelion herb with r...	20531	6
Galke	Dandelion herb with r...	22093	2
Gehe	Dandelion herb with r...	6611B110104	1
Gehe	Dandelion herb with r...	13019803	1
Hedinger	Dandelion herb with r...	10121614	1
Klenk	Dandelion herb with r...	6611B110131	1
Klenk	Dandelion herb with r...	6611B160613	1
Klenk	Dandelion herb with r...	6611B120620	19
Klenk	Dandelion herb with r...	6611A110104	1
Klenk	Dandelion herb with r...	6611B130314	3
Klenk	Dandelion herb with r...	5122013b	1
Klenk	Dandelion herb with r...	6611B1104104	1
Klenk	Dandelion herb with r...	6611B090306	1
Klenk	Dandelion herb with r...	6611B-120620	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Dandelion herb with r...	6611B-131206	1
Klenk	Dandelion herb with r...	6611B110104	5
Klenk	Dandelion herb with r...	6611B110929	2
Bombastus	Dandelion herb with r...	277597	6
Phönix	Dandelion herb with r...	6611B130321	29
Sanacorp	Dandelion herb with r...	13108803	2
Caelo	Dandelion herb with r...	10121602	1
Caelo	Dandelion herb withou...	11217107	1
Caelo	Dandelion herb withou...	11030311	1
Caelo	Dandelion herb withou...	7031305	1
Caelo	Dandelion herb withou...	11371904	2
Caelo	Dandelion herb withou...	11217109	1
Caelo	Dandelion herb withou...	1127102	1
Caelo	Dandelion herb withou...	13091305	1
Caelo	Dandelion herb withou...	11371907	1
Caelo	Dandelion herb withou...	11371902	1
Caelo	Dandelion herb withou...	1137907	1
Caelo	Dandelion herb withou...	9011403	1
Caelo	Dandelion herb withou...	107063	1
Caelo	Dandelion root, cut	12363104	3
Caelo	Dandelion root, cut	10024710	1
Caelo	Dandelion root, cut	11003307	1
Caelo	Dandelion root, cut	11003311	2
Caelo	Dandelion root, cut	12363102	2
Caelo	Dandelion root, cut	12363103	1
Caelo	Dandelion root, cut	12363107	1
Caelo	Dandelion root, cut	12367916	1
Caelo	Dandelion root, cut	12363109	2
Caelo	Dandelion root, cut	12363108	2
Caelo	Dandelion root, cut	12363110	1
Caelo	Dandelion root, cut	13329705	1
Caelo	Dandelion root, cut	14166502	1
Caelo	Dandelion root, cut	15407703	1
Caelo	Dandelion root, cut	16161308	1
Caelo	Dandelion root, cut	15407703	1
Caelo	Dandelion root, cut	13329702	8
Caelo	Dandelion root, cut	16161303	1
Caelo	Dandelion root, cut	14166504	1
Caelo	Dandelion root, cut	14376602	1
Caelo	Dandelion root, cut	12363106	1
Caelo	Dandelion root, cut	11003313	1
Caelo	Dandelion root, cut	14166501	1
Caelo	Dandelion root, cut	14376603	1
Galke	Dandelion root, cut	126302	1
Galke	Dandelion root, cut	20658	1
Caelo	Dandelion root, cut	1140317	1
Klenk	Dandelion root, cut	6621A120208	6
Klenk	Dandelion root, cut	6621A110420	1
Klenk	Dandelion root, cut	6101202	1
Klenk	Dandelion root, cut	A120606	1
Klenk	Dandelion root, cut	N130813	1
Klenk	Dandelion root, cut	6621B170112	1
Klenk	Dandelion root, cut	6621N130813	6
Klenk	Dandelion root, cut	6621A140114	3
Klenk	Dandelion root, cut	6621A140114	3
Klenk	Dandelion root, cut	6621A160111	1
Klenk	Dandelion root, cut	6621A120606	15
Klenk	Dandelion root, cut	6621A141027	5
noweda	Dandelion root, cut		1
Euro OTC	Deoxycholic acid	1305051-01	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Deoxycholic acid	13J21-N14	1
Gehe	Deoxycholic acid	2012060253	1
GEHE 21.10.2014	Deoxycholic acid	13F13-N06	1
Caelo	Devil's claw root	12031806	1
Caelo	Devil's claw root	12031810	1
Caelo	Devil's claw root	12031809	1
Caelo	Devil's claw root	12031811	1
Caelo	Devil's claw root	6331B110426	2
Caelo	Devil's claw root	12031803	1
Galke	Devil's claw root	20282	2
Galke	Devil's claw root	21018	2
Gehe	Devil's claw root	1114005	1
Klenk	Devil's claw root	10111204	1
Klenk	Devil's claw root	6331B130129	5
Klenk	Devil's claw root	6331B120508	3
Fagron	Dexamethasone 1:10 (r...	12K06-N09	1
Fagron	Dexamethasone 1:10 (r...	11g08-n02	1
Fagron	Dexamethasone 1:10 (r...	12e30-n16	2
Fagron	Dexamethasone 1:10 (r...	12C20-N03	4
Fagron	Dexamethasone 1:10 (r...	12L19-N06	1
Caelo	Dexamphetamine sulfate	C9H13N14	1
Fagron	Dexamphetamine sulfate	11F29-N01	1
Fagron	Dexamphetamine sulfate	17B09-B02-339689	2
Fagron	Dexamphetamine sulfate	17B09-B02-339690	1
Fagron	Dexamphetamine sulfate	15H06-B04-313861	1
Fargon/Gehe	Dexamphetamine sulfate	15H06-B04	1
Caelo	Dihydrocodeine hydrog...	12142503	2
Caelo	Dihydrocodeine hydrog...	12142508	2
Caelo	Dihydrocodeine hydrog...	13267603	1
Caelo	Dihydrocodeine hydrog...	13267604	2
Caelo	Dihydrocodeine hydrog...	13267608	1
Caelo	Dihydrocodeine hydrog...	15295903	2
Caelo	Dihydrocodeine hydrog...	16106202	5
Caelo	Dihydrocodeine hydrog...	15F18-B07-322054	1
Caelo	Dihydrocodeine hydrog...	18115205	2
Caelo	Dihydrocodeine hydrog...	15295905	4
Caelo	Dihydrocodeine hydrog...	15295907	1
Caelo	Dihydrocodeine hydrog...	16106203	4
Caelo	Dihydrocodeine hydrog...	17097508	2
Caelo	Dihydrocodeine hydrog...	18115202	3
Fagron	Dihydrocodeine hydrog...	12G05-N01	1
Fagron	Dihydrocodeine hydrog...	13H19-N08	3
Fagron	Dihydrocodeine hydrog...	14D08-B06	1
Fagron	Dihydrocodeine hydrog...	14K26-B04	1
Fagron	Dihydrocodeine hydrog...	14K26-B04-317257	1
Fagron	Dihydrocodeine hydrog...	15F18-B07	1
Fagron	Dihydrocodeine hydrog...	15F18-B07-323388	1
Fagron	Dihydrocodeine hydrog...	15F18B07	2
Fagron	Dihydrocodeine hydrog...	16I27-B03-332122	1
Fagron	Dihydrocodeine hydrog...	16-00326	1
Fagron	Dihydrocodeine hydrog...	16I27-B03	1
Fagron	Dihydrocodeine hydrog...	17G04-B02-342861	1
Fagron	Dihydrocodeine hydrog...	17G04-B02	1
Fagron	Dihydrocodeine hydrog...	14K26-B04-310974	1
Caelo	Dihydrocodeine hydrog...	17097502	2
Hedinger	Dihydrocodeine hydrog...	70162	4
Th. Geyer	Dihydrocodeine hydrog...	59819	1
Th. Geyer	Dihydrocodeine hydrog...	67052	10
Th. Geyer	Dihydrocodeine hydrog...	20170808-03065	1
Th. Geyer	Dihydrocodeine hydrog...	67035	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Akazie	Dill fruit	20.09.2015	1
Caelo	Dill fruit	12289901	1
Caelo	Dill fruit	12038302	2
Caelo	Dill fruit	12342901	2
Caelo	Dill fruit	12342904	7
Caelo	Dill fruit	12342903	1
Caelo	Dill fruit	12342908	2
Caelo	Dill fruit	12038304	4
Caelo	Dill fruit	9189003	1
Caelo	Dill fruit	16040406	1
Caelo	Dill fruit	12342906	2
Galke	Dill fruit	22422	4
Hepart AG	Dill fruit	L30057kba	1
Klenk	Dill fruit	2680A-120312	1
Klenk	Dill fruit	2680A120312	7
Klenk	Dill fruit	A120312	1
Klenk	Dill fruit	2680A121211	3
Klenk	Dill fruit	2680a120312	1
Kräuter Schulte	Dill fruit	6363	1
Caelo	Dill fruit	16348702	2
Caelo	Dill fruit	16348707	1
Caelo	Dill fruit	12342909	5
Wolf	Dill fruit	E-501	1
Wolf	Dill fruit	L30057	5
Wolf	Dill fruit	23622	6
Bombastus	Dill herb, cut	50836505	1
Caelo	Dill herb, cut	11295109	1
Caelo	Dill herb, cut	13007601	1
Caelo	Dill herb, cut	13007605	1
Caelo	Dill herb, cut	15178603	1
Caelo	Dill herb, cut	13007602	1
Caelo	Dill herb, cut	13007608	1
Klenk	Dill herb, cut	3531B110726	1
Dr. Behr	Dimercaptosuccinic acid	WE14020002	1
Euro OTC	Diphenylcyclopropenone	17B-13B02-334769	1
Fagron	Diphenylcyclopropenone	16F02-B10-327812	3
Fagron	Diphenylcyclopropenone	18I03B04	1
Fagron	Diphenylcyclopropenone	1 (17B13-B02-34977)	1
Fagron	Diphenylcyclopropenone	16F02B10324263	1
Fagron	Diphenylcyclopropenone	35-16-I-95P3117	1
Fiebig	Diphenylcyclopropenone	17B13-B02-334769	1
Frago/Noweda	Diphenylcyclopropenone	16F02-B10-324263	2
Fagron	Diphenylcyclopropenone	18I03-B04_356833	1
Falcento	D-ribose	201206712	2
Falcento	D-ribose	201209702	1
Falcento	D-ribose	JXCZSJ14-D-010	1
Unisan	D-ribose	JXCZSJ13D-013	2
Fagron	Drofenine hydrochloride	12D04-N03	1
Fagron	Drofenine hydrochloride	11J24-N01	1
Caelo	Dry beads Caelo ora...	11005811	1
Kräuter Schulte	Dryas octopetala herb...	38970	1
Caelo	Echinacea pallida roo...	11115206	1
Caelo	Echinacea pallida roo...	12244504	1
Caelo	Econazole nitrate	ECN140301	1
Fagron	Econazole nitrate	13D22-N06	1
Fagron	Econazole nitrate	11F09-N16	1
Fagron	Econazole nitrate	14G22-B07-306926	1
Caelo	Elder berries	12267801	1
Gehe	Elder berries	12267807	1
Klenk	Elder berries	3010N120921	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Elder flower, rubbed	275393	4
Bahnhof-Apotheke	Elder flower, rubbed	17-121112	1
Bombastus	Elder flower, rubbed	265631	1
Bombastus	Elder flower, rubbed	279216	3
Caelo	Elder flower, rubbed	12221902	10
Caelo	Elder flower, rubbed	10291308	2
Caelo	Elder flower, rubbed	10291312	2
Caelo	Elder flower, rubbed	12221904	10
Caelo	Elder flower, rubbed	1571a121022	1
Caelo	Elder flower, rubbed	31051301	1
Caelo	Elder flower, rubbed	12221905	7
Caelo	Elder flower, rubbed	12221906	1
Caelo	Elder flower, rubbed	12221907	4
Caelo	Elder flower, rubbed	14111317	1
Caelo	Elder flower, rubbed	5122013d	1
Caelo	Elder flower, rubbed	12221909	1
Caelo	Elder flower, rubbed	13244601	4
Caelo	Elder flower, rubbed	13244602	2
Caelo	Elder flower, rubbed	12221910	2
Caelo	Elder flower, rubbed	1571A121022	14
Caelo	Elder flower, rubbed	10291309	3
Caelo	Elder flower, rubbed	12221904-3360319071	1
Caesar/Noweda	Elder flower, rubbed	4910A-01471	1
Finze	Elder flower, rubbed	9297415	1
Galke	Elder flower, rubbed	21934	1
Gehe	Elder flower, rubbed	1250213	1
Gehe	Elder flower, rubbed	1090413	1
Klenk	Elder flower, rubbed	1571A141126	1
Klenk	Elder flower, rubbed	1571A110223	16
Klenk	Elder flower, rubbed	16061201	1
Klenk	Elder flower, rubbed	26061201	1
Klenk	Elder flower, rubbed	21091201	1
Klenk	Elder flower, rubbed	1571A110125	2
Klenk	Elder flower, rubbed	13021301	1
Klenk	Elder flower, rubbed	1571A121121	20
Klenk	Elder flower, rubbed	1571A1202015	1
Klenk	Elder flower, rubbed	A121121	1
Klenk	Elder flower, rubbed	A120215	1
Klenk	Elder flower, rubbed	1571A130627	2
Klenk	Elder flower, rubbed	1571A-110223	1
Klenk	Elder flower, rubbed	1571a120215	1
Klenk	Elder flower, rubbed	1571A130930	3
Klenk	Elder flower, rubbed	1571a1211	1
Klenk	Elder flower, rubbed	1571A120215	4
Caelo	Elder flower, rubbed	1029310	1
Bombastus	Elder flower, rubbed	269873	2
Caelo	Elder flower, rubbed	10291310	5
Wolf	Elder flower, rubbed	E-738	1
Wolf	Elder flower, rubbed	22749	1
Wolf	Elder flower, rubbed	22765	1
Wolf	Elder flower, rubbed	B-810	1
Klenk	Elder root, cut	6281B110427	4
Probe	Elder root, cut	12345	1
-	Elecampane rhizome, cut	712M-02181	1
Caelo	Elecampane rhizome, cut	12113304	3
Caelo	Elecampane rhizome, cut	1211334	1
Caelo	Elecampane rhizome, cut	6341B	1
Caelo	Elecampane rhizome, cut	11374702	1
Caelo	Elecampane rhizome, cut	13152402	1
Caelo	Elecampane rhizome, cut	13152401	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Elecampane rhizome, cut	12113303	1
Galke	Elecampane rhizome, cut	21569	2
Gehe	Elecampane rhizome, cut	11196906	1
Gehe	Elecampane rhizome, cut	12113302	2
Caelo	Elecampane rhizome, cut	11374703	1
Klenk	Elecampane rhizome, cut	6341B100426	2
Klenk	Elecampane rhizome, cut	6341B120611	2
Klenk	Elecampane rhizome, cut	B130423	3
Klenk	Elecampane rhizome, cut	6341B130423	3
Klenk	Elecampane rhizome, cut	6311141B130423	1
Noweda	Elecampane rhizome, cut	6341B111118	3
Caelo	Elecampane rhizome, cut	13152403	2
Richter	Elecampane rhizome, cut	P158683	1
Caelo	Eleutherococcus, cut	10381818	2
Caelo	Eleutherococcus, cut	12326703	1
Caelo	Eleutherococcus, cut	10381817	1
Caelo	Eleutherococcus, cut	12326707	1
Klenk	Eleutherococcus, cut	7011A121204	1
Klenk	Eleutherococcus, cut	7011A101206	1
Klenk	Eleutherococcus, cut	7011A110714	1
Caelo	Eleutherococcus, cut	12326701	1
Caelo	Elm bark, cut	10347204	1
Caelo	Elm bark, cut	12287902	2
Caelo	Elm bark, cut	10347203	1
Klenk	Elm bark, cut	841a120413	1
Klenk	Elm bark, cut	841A1101120	1
Aurica / 11	Equisetum stem, cut	521302898	1
Bomba/AHD	Equisetum stem, cut	280449	3
Bombastus	Equisetum stem, cut	273963	1
Bombastus	Equisetum stem, cut	275891	3
Bombastus	Equisetum stem, cut	264100	1
Bombastus	Equisetum stem, cut	272552	2
Bombastus	Equisetum stem, cut	265924	1
Bombastus	Equisetum stem, cut	278107	1
Bombastus	Equisetum stem, cut	18111304	1
Bombastus	Equisetum stem, cut	6011401	1
Bombastus	Equisetum stem, cut	280647	1
Bombastus	Equisetum stem, cut	268321	1
Bombastus	Equisetum stem, cut	264101	1
Bombastus	Equisetum stem, cut	274714	1
Caelo	Equisetum stem, cut	13344309	3
Caelo	Equisetum stem, cut	11021901	1
Caelo	Equisetum stem, cut	11076302	2
Caelo	Equisetum stem, cut	3091201	1
Caelo	Equisetum stem, cut	11076306	6
Caelo	Equisetum stem, cut	8101201	1
Caelo	Equisetum stem, cut	17101203	1
Caelo	Equisetum stem, cut	20111212	1
Caelo	Equisetum stem, cut	11076303	13
Caelo	Equisetum stem, cut	2658181	1
Caelo	Equisetum stem, cut	10328901	1
Caelo	Equisetum stem, cut	1288804	1
Caelo	Equisetum stem, cut	8041301	1
Caelo	Equisetum stem, cut	8051302	1
Caelo	Equisetum stem, cut	12288802	2
Caelo	Equisetum stem, cut	6081304	1
Caelo	Equisetum stem, cut	311042	1
Caelo	Equisetum stem, cut	13159702	10
Caelo	Equisetum stem, cut	13159706	5
Caelo	Equisetum stem, cut	13091301	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Equisetum stem, cut	13159704	6
Caelo	Equisetum stem, cut	9101313	1
Caelo	Equisetum stem, cut	30101305	1
Caelo	Equisetum stem, cut	13344305	1
Caelo	Equisetum stem, cut	2011408	1
Caelo	Equisetum stem, cut	13344304	5
Caelo	Equisetum stem, cut	13344311	1
Caelo	Equisetum stem, cut	13350301	1
Caelo	Equisetum stem, cut	13350309	1
Caelo	Equisetum stem, cut	15015404	1
Caelo	Equisetum stem, cut	10328915	1
Caelo	Equisetum stem, cut	11021904	1
Caelo	Equisetum stem, cut	11076307	1
Caelo	Equisetum stem, cut	12288808	9
Caelo	Equisetum stem, cut	282573	1
Caelo	Equisetum stem, cut	13200201	1
Caelo	Equisetum stem, cut	10375520	1
Caelo	Equisetum stem, cut	13159705-3387310190	1
Caelo	Equisetum stem, cut	13153702	1
Caelo	Equisetum stem, cut	1359702	1
Caelo	Equisetum stem, cut	13159705	6
Caelo	Equisetum stem, cut	13344303	6
Caelo	Equisetum stem, cut	12288809	3
Caelo	Equisetum stem, cut	13159702-3464312101	1
Caelo	Equisetum stem, cut	13344302	3
Caesar & Loretz GmbH,...	Equisetum stem, cut	10375510	2
Caesar & Loretz GmbH,...	Equisetum stem, cut	12288801	16
Euro OTC	Equisetum stem, cut	3831A130610	5
Finze	Equisetum stem, cut	11076305	8
Galke	Equisetum stem, cut	19663	5
Galke	Equisetum stem, cut	22061	1
Gehe	Equisetum stem, cut	10375515	1
Gehe	Equisetum stem, cut	11076301	4
Gehe	Equisetum stem, cut	12288803	14
Klenk	Equisetum stem, cut	3831A111124	4
Hepart AG	Equisetum stem, cut	B-695, kBA	1
Hubertus Apotheke	Equisetum stem, cut	3831C140403	1
KBA Ware	Equisetum stem, cut	21879	6
Klenk	Equisetum stem, cut	3831a120611	1
Klenk	Equisetum stem, cut	2213U01642	1
Klenk	Equisetum stem, cut	3831A121018	6
Klenk	Equisetum stem, cut	3831A120903	8
Klenk	Equisetum stem, cut	3831A110922	1
Klenk	Equisetum stem, cut	3831A120018	1
Klenk	Equisetum stem, cut	3831A1230726	1
Klenk	Equisetum stem, cut	3831c131104	1
Klenk	Equisetum stem, cut	3831C131104	1
Klenk	Equisetum stem, cut	3831A11124	1
Klenk	Equisetum stem, cut	4713U01642	1
Klenk	Equisetum stem, cut	3831A110601	1
Klenk	Equisetum stem, cut	3831A120529	8
Klenk	Equisetum stem, cut	4413Q1642	1
Klenk	Equisetum stem, cut	3831A120611	10
Noweda	Equisetum stem, cut	12231401	6
Klenk	Equisetum stem, cut	3831A120726	18
Caelo	Equisetum stem, cut	13344306	1
Caelo	Equisetum stem, cut	12288804	11
Phönix	Equisetum stem, cut	12288807	2
Sanacorp	Equisetum stem, cut	13344307	1
Caelo	Equisetum stem, cut	10375507	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Equisetum stem, cut		2
Wolf	Equisetum stem, cut	B-695	1
Wolf	Equisetum stem, cut	B233885	4
apomix	Ergotamine tartrate	15L01-B02	1
Fagron	Ergotamine tartrate	15B16-B05-308417	1
Fagron	Ethyl hydrogen fumara...	14H27-B04-299502	6
Caelo	Eucalyptus leaf, cut	12225203	3
Klenk	Eucalyptus leaf, cut	2011B120419	6
Caelo	Eucalyptus leaf, cut	9346811	1
Caelo	Eucalyptus leaf, cut	12225202	1
Caelo	Eucalyptus leaf, cut	122250204	1
Caelo	Eucalyptus leaf, cut	12225206	1
Caelo	Eucalyptus leaf, cut	11307708	2
Klenk	Eucalyptus leaf, cut	B120419	1
Klenk	Eucalyptus leaf, cut	B130306	2
Klenk	Eucalyptus leaf, cut	2011B130306	4
Klenk	Eucalyptus leaf, cut	2011b130306	1
Klenk	Eucalyptus leaf, cut	2011B130306-35294110	1
VDL	Eucalyptus leaf, cut	2011B110801	4
Bombastus	Euphrasy herb, cut	274553	1
Bombastus	Euphrasy herb, cut	270726	2
Bombastus	Euphrasy herb, cut	278108	2
Bombastus	Euphrasy herb, cut	277846	1
Caelo	Euphrasy herb, cut	112211643	1
Caelo	Euphrasy herb, cut	11030810	1
Caelo	Euphrasy herb, cut	29011302	1
Caelo	Euphrasy herb, cut	12103202	9
Caelo	Euphrasy herb, cut	12103203	10
Caelo	Euphrasy herb, cut	7051302	1
Caelo	Euphrasy herb, cut	312052	1
Caelo	Euphrasy herb, cut	13180001	5
Caelo	Euphrasy herb, cut	30101307	1
Caelo	Euphrasy herb, cut	13180004	5
Caelo	Euphrasy herb, cut	12103201	1
Caelo	Euphrasy herb, cut	13180005	2
Caelo	Euphrasy herb, cut	8011419	1
Caelo	Euphrasy herb, cut	13180008	1
Caelo	Euphrasy herb, cut	14019107	1
Caelo	Euphrasy herb, cut	1213202	1
Caelo	Euphrasy herb, cut	14019102	2
Caelo	Euphrasy herb, cut	13180002	5
Caelo	Euphrasy herb, cut	11030812	4
Galke	Euphrasy herb, cut	20262	2
Klenk	Euphrasy herb, cut	15029806	1
Klenk	Euphrasy herb, cut	B101206	1
Klenk	Euphrasy herb, cut	B130430	1
Klenk	Euphrasy herb, cut	3871B130430	1
Caelo	Euphrasy herb, cut	11030811	3
Caelo	European golden rod, ...	13386908	1
Caelo	European golden rod, ...	12343102	1
Caelo	European golden rod, ...	12343103-3466312121	1
Klenk	European golden rod, ...	1781B110706	1
Kenk / Phoenix	European golden rod, ...	1781B110826	1
Sanacorp	European golden rod, ...	12343103	1
Fagron	Fentanyl citrate	20100911-1	1
Fagron	Fentanyl citrate	10H20-N02	1
Fagron	Fentanyl citrate	18L27-B03-525913	1
Apofit	Fenugreek	222392	1
Caelo	Fenugreek	12252601	2
Caelo	Fenugreek	11313203	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Fenugreek	13013801	1
Caelo	Fenugreek	1131206	1
Caelo	Fenugreek	12252603	3
Caelo	Fenugreek	13013803	6
Caelo	Fenugreek	13013805	3
Gehe	Fenugreek	11313204	1
Gehe	Fenugreek	13013811	2
Klenk	Fenugreek	7260A130603	3
Klenk	Fenugreek	9011301	1
Klenk	Fenugreek	A120118	2
Klenk	Fenugreek	8061301	1
Klenk	Fenugreek	A130603	1
Klenk	Fenugreek	7260A110530	2
Klenk	Fenugreek	7260A120118	2
Phoenix	Fenugreek	11313206	7
Caelo	Fenugreek	12252602	2
Caelo	Fenugreek, powdered	12149605	1
Caelo	Fenugreek, powdered	12149607	1
Caelo	Fenugreek, powdered	13398302	1
Caelo	Fenugreek, powdered	15308703	2
Caelo	Fenugreek, powdered	7264a110201	2
Caelo	Fenugreek, powdered	14057807	1
Caelo	Fenugreek, powdered	14377201	2
Caelo	Fenugreek, powdered	14057801	1
Fagron	Fenugreek, powdered	12149603	1
Ichthyol/Phoenix	Fenugreek, powdered	14377205	1
Klenk	Fenugreek, powdered	A110201	1
Klenk	Fenugreek, powdered	12082014A	1
Klenk	Fenugreek, powdered	7264A110201	9
Klenk	Fenugreek, powdered	7264B150303	1
Nachprüfung	Fenugreek, powdered	2412E02239	1
Caelo	Feverfew herb, cut	12380204	1
Caelo	Feverfew herb, cut	12380203	5
Sanacorp	Feverfew herb, cut	12380201	2
Caelo	Flax weed herb, cut	11104507	8
Caelo	Flax weed herb, cut	13007502	2
Caelo	Flax weed herb, cut	13007505	1
Caelo	Flax weed herb, cut	14005303	1
Caelo	Flax weed herb, cut	14005305	3
Caelo	Flax weed herb, cut	14197204	1
Caelo	Flax weed herb, cut	16292809	1
Caelo	Flax weed herb, cut	16292801	1
Caelo	Flax weed herb, cut	11104505	1
Caelo	Flax weed herb, cut	13007507	7
Klenk	Flax weed herb, cut	4011B131115	3
Klenk	Flax weed herb, cut	4011B121207	2
Bombastus	Frangula bark, cut	268407	1
Bombastus	Frangula bark, cut	270733	1
Bombastus	Frangula bark, cut	273926	1
Bombastus	Frangula bark, cut	275998	2
Bombastus	Frangula bark, cut	281284	2
Bombastus	Frangula bark, cut	278599	3
Bombastus	Frangula bark, cut	238812	1
Caelo	Frangula bark, cut	11254001	2
Caelo	Frangula bark, cut	11340801	1
Caelo	Frangula bark, cut	12185901	10
Caelo	Frangula bark, cut	10061301	1
Caelo	Frangula bark, cut	13203008	1
Caelo	Frangula bark, cut	6011402	1
Caelo	Frangula bark, cut	14163102	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Frangula bark, cut	eztetdt	1
Caelo	Frangula bark, cut	12186001	1
Caelo	Frangula bark, cut	12186003	1
Caelo	Frangula bark, cut	12186006	7
Caelo	Frangula bark, cut	12186005	1
Caelo	Frangula bark, cut	1286003	1
Caelo	Frangula bark, cut	12186002	15
Caelo	Frangula bark, cut	121860006	1
Caesar&lorenz,Phoenix	Frangula bark, cut	14163104	1
Finze	Frangula bark, cut	249091	1
Gehe	Frangula bark, cut	11254003	2
Gehe	Frangula bark, cut	11254004	4
Gehe	Frangula bark, cut	11254006	4
Klenk	Frangula bark, cut	661B110412	4
Klenk	Frangula bark, cut	6621B110412	1
Klenk	Frangula bark, cut	661B130306	1
Klenk	Frangula bark, cut	661B-090903	1
Klenk	Frangula bark, cut	661B-110412	1
Caelo	Frangula bark, cut	12186004	11
Caelo	Frankincense	12120005	5
Caelo	Frankincense	10349210	1
Caelo	Frankincense	10349213	1
Caelo	Frankincense	12120008	2
Caelo	Frankincense	13112801	5
Caelo	Frankincense	13112809	2
Caelo	Frankincense	4614M-02030	1
Caelo	Frankincense	15140810	1
Caelo	Frankincense	15140809	1
Caelo	Frankincense	15140805	2
Caelo	Frankincense	15140804	1
Caelo	Frankincense	12120006	3
Caelo	Frankincense	13112803	1
Caelo	Frankincense	13112807	1
Caelo	Frankincense	14107803	2
Caelo	Frankincense	12120012-3421310191	1
Caelo	Frankincense	13112803-3494411030	1
Fagron	Frankincense		1
Gahlke	Frankincense	21949	1
vedono	Frankincense	12120009	5
vedono	Frankincense	12120012	1
Euro OTC	Frankincense extract ...	1104005V-04	2
Klenk	Fraxinella root, cut	6271B140708	1
Fagron	Fuchsine	12A03-N06	1
Fagron	Fuchsine	12F28-N02	1
Fagron	Fuchsine	12G18-N01	1
Fagron	Fuchsine	13H23-M04	2
Fagron	Fuchsine	13A30-N05	1
Caelo	Fumitory, cut	11101406	1
Caelo	Fumitory, cut	11101410	1
Caelo	Fumitory, cut	11101411	3
Caelo	Fumitory, cut	11101413	3
Caelo	Fumitory, cut	31081201	1
Caelo	Fumitory, cut	7111201	1
Caelo	Fumitory, cut	13202902	11
Caelo	Fumitory, cut	13202905	2
Caelo	Fumitory, cut	12103408	5
Caelo	Fumitory, cut	12103405	7
Caelo	Fumitory, cut	11101408	1
Caelo	Fumitory, cut	12103404	2
Caelo	Fumitory, cut	12103407	6

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Fumitory, cut	1320902	1
Caelo	Fumitory, cut	72878477	1
Caelo	Fumitory, cut	8312901	1
Gehe	Fumitory, cut	12103402	2
Kenk / Phoenix	Fumitory, cut	3881B111013	2
Klenk	Fumitory, cut	B120410	1
Klenk	Fumitory, cut	3881B100127	1
Caelo	Galangal root	12330305	1
Caelo	Galangal root	11375904	1
Caelo	Galangal root	12330306	2
Caelo	Galangal root	15128008	1
Caelo	Galangal root	16196901	1
Caelo	Galangal root	16196904	1
Caelo	Galangal root	12125004	2
Caelo	Galangal root	1215004	1
Caelo	Galangal root	12330303	1
Caelo	Galangal root	15045701	1
Gehe	Galeopsis herb, cut	3911A130320	6
Klenk	Galeopsis herb, cut	3911A080409	1
Klenk	Galeopsis herb, cut	3911A130110	3
Klenk	Galeopsis herb, cut	3911A090219	2
Klenk	Galeopsis herb, cut	3911a130320	1
Caelo	Garden violet, cut	11124008	1
Caelo	Garden violet, cut	13038701	4
Caelo	Garden violet, cut	11124007	1
Caelo	Garden violet, cut	1303872	1
Caelo	Garden violet, cut	13038703	2
Caelo	Garden violet, cut	10011403	1
Caelo	Garden violet, cut	13232107	1
Caelo	Garden violet, cut	11124007-3284310662	1
an	Gentian root, cut	6311b130305	1
Anzag EK7,91 08.08.12	Gentian root, cut	10263407	1
Caelo	Gentian root, cut	10263404	1
Caelo	Gentian root, cut	10263411	1
Caelo	Gentian root, cut	30011301	1
Caelo	Gentian root, cut	19071304	1
Caelo	Gentian root, cut	Int.Ch:313091	1
Caelo	Gentian root, cut	12244608	1
Caelo	Gentian root, cut	6311B130305	2
Caelo	Gentian root, cut	13156102	1
Caelo	Gentian root, cut	12244607	1
Caesar & Loretz GmbH,...	Gentian root, cut	12244603	2
Galke	Gentian root, cut	19192	2
Klenk	Gentian root, cut	6311B130205	2
Klenk	Gentian root, cut	6311B140704	1
Klenk	Gentian root, cut	6311A120723	3
Klenk	Gentian root, cut	6311a120723	2
Klenk	Gentian root, cut	1911E-02142	1
kräuter schulte	Gentian root, cut	52348	1
Phoenix	Gentian root, cut	6311B120104	1
Phönix	Gentian root, cut	269197	2
Phönix	Gentian root, cut	6311B120315	8
Richter	Gentian root, cut	P200907	1
-	Gentian root, powdered	130063	1
Caelo	Gentian root, powdered	15011403	1
Caelo	Gentian root, powdered	14215601	1
Caelo	Gentian root, powdered	12007106	1
Galke	Geum urbanum herb, cut	20881	1
Kräuter Schulte	Geum urbanum herb, cut	51737	1
Caelo	Ginger, peeled	11325715	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Ginger, peeled	11325716	1
Caelo	Ginger, peeled	19121201	1
Caelo	Ginger, peeled	11325719	3
Caelo	Ginger, peeled	13100602	2
Caelo	Ginger, peeled	13310604	4
Caelo	Ginger, peeled	12180604	1
Caelo	Ginger, peeled	13100604	1
Caelo	Ginger, peeled	11325703	2
Caelo	Ginger, peeled	11325712	1
Caelo	Ginger, peeled	13100605	4
Caelo	Ginger, peeled	13310602	2
Caelo	Ginger, peeled	12164911-3368319002	1
Galke	Ginger, peeled	20633	1
Galke	Ginger, peeled	21766	2
Klenk	Ginger, peeled	6951B110119	1
Klenk	Ginger, peeled	6951B110822	1
Klenk	Ginger, peeled	6951B100302	1
Klenk	Ginger, peeled	6951B130110	1
Phönix	Ginger, peeled	13310601	1
Richter	Ginger, peeled	KR27992	1
Caelo	Ginger, peeled, powde...	12164901	1
Caelo	Ginger, peeled, powde...	13092013B	1
Caelo	Ginger, peeled, powde...	12164911	1
Klenk	Ginger, peeled, powde...	6954B16029	1
Klenk	Ginger, peeled, powde...	6954B170127	1
Klenk	Ginger, peeled, powde...	6954B110801	1
Klenk	Ginger, peeled, powde...	B121030	2
Klenk	Ginger, peeled, powde...	6954B130418	2
Klenk	Ginger, peeled, powde...	6954B121030	2
Klenk	Ginger, peeled, powde...	6954B160429	5
Klenk	Ginger, peeled, powde...	KS200260	1
Klenk	Ginger, peeled, powde...	6954B160929	2
Caelo	Ginkgo leaf, cut	12151709	2
Caelo	Ginkgo leaf, cut	15077407	1
Caelo	Ginkgo leaf, cut	13340907	1
Caelo	Ginkgo leaf, cut	13340904	1
Caelo	Ginkgo leaf, cut	13340906	1
Caelo	Ginkgo leaf, cut	12373604	1
Nachprüfung	Ginkgo leaf, cut	2461A100429	10
Bombastus	Ginseng root	13150903	1
Caelo	Ginseng root	13341001	1
Caelo	Ginseng root	12080218	1
Caelo	Goat's rue, cut	11307903	1
Caelo	Goat's rue, cut	11175104	1
Caelo	Goat's rue, cut	11307901	1
Caelo	Goat's rue, cut	12017907	3
Caelo	Goat's rue, cut	12017914	1
Caelo	Goat's rue, cut	12017913	2
Caelo	Goat's rue, cut	12343303	6
Caelo	Goat's rue, cut	12343302	4
Caelo	Goat's rue, cut	5122013e	1
Caelo	Goat's rue, cut	12343305	3
Caelo	Goat's rue, cut	12343308	1
Galke	Goat's rue, cut	8378	2
Klenk	Goat's rue, cut	3901C110905	1
Klenk	Goat's rue, cut	3901B140801	1
Caelo	Goat's rue, cut	12017912	1
Sanacorp	Goat's rue, cut	12017911	1
Caelo	Ground ivy herb, cut	11052315	1
Caelo	Ground ivy herb, cut	11052314	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Ground ivy herb, cut	11374611	2
Caelo	Ground ivy herb, cut	11374615	1
Caelo	Ground ivy herb, cut	11374606	1
Caelo	Ground ivy herb, cut	11374602	1
Caelo	Ground ivy herb, cut	11374609	1
Caelo	Ground ivy herb, cut	11052318	2
Gutenberg-Apotheke	Ground ivy herb, cut	11374610	3
Klenk	Ground ivy herb, cut	3991B110304	1
Klenk	Ground ivy herb, cut	3991B130502	2
Phönix	Ground ivy herb, cut	11374608	1
Richter	Ground ivy herb, cut	s99/09	1
Caelo	Guaiacum wood, cut	11352001	1
Caelo	Guaiacum wood, cut	4011M-01778	1
Caelo	Guaiacum wood, cut	11352008	1
Caelo	Guaiacum wood, cut	8041401	1
Caelo	Guaiacum wood, cut	16136708	1
Caelo	Guaiacum wood, cut	11352010	1
Caelo	Guaiacum wood, cut	14008203	1
Caelo	Guaiacum wood, cut	16136710	1
Caelo	Guaiacum wood, cut	16136706	1
Caelo	Guaiacum wood, cut	11352012	1
sana 09.12.14 3,75	Guaiacum wood, cut	13343802	1
Caelo	Hamamelis bark, cut	12361301	1
Caelo	Hamamelis bark, cut	13123701	1
Caelo	Hamamelis bark, cut	13123703	1
Caelo	Hamamelis leaf, cut	10102915	1
Caelo	Hamamelis leaf, cut	12165805	1
Caelo	Hamamelis leaf, cut	12164802	1
Caelo	Hamamelis leaf, cut	14356103	1
Caelo	Hamamelis leaf, cut	13269904	1
Caelo	Hamamelis leaf, cut	13269902	2
Caelo	Hamamelis leaf, cut	12164804	1
Euro OTC	Hamamelis leaf, cut	12164805	1
Klenk	Hamamelis leaf, cut	B110214	1
Klenk	Hamamelis leaf, cut	2051B110214	1
Caelo	Hamamelis leaf, cut	13269905	1
Alliance	Hawthorn flower	13010403	1
Caelo	Hawthorn flower	13010403	5
Caelo	Hawthorn flower	7121201	1
Caelo	Hawthorn flower	11068208	1
Caelo	Hawthorn flower	13010402	2
Caelo	Hawthorn flower	11068209	1
Caelo	Hawthorn flower	13010402	3
Caelo	Hawthorn flower	11068202	1
Caelo	Hawthorn flower	21051301	1
Caelo	Hawthorn flower	25101301	1
Caelo	Hawthorn flower	13253303	1
Caelo	Hawthorn flower	11068206	1
Caelo	Hawthorn flower	13253304	1
Caelo	Hawthorn flower	1351B130819	3
Caesar & Loretz GmbH	Hawthorn flower	11068206	3
Hepart AG	Hawthorn flower	13010401	1
Klenk	Hawthorn flower	1351B111207	4
Klenk	Hawthorn flower	B1112107	1
Caelo	Hawthorn fruit	11278202	1
Caelo	Hawthorn fruit	12326308	1
Caelo	Hawthorn fruit	13101402	2
Caelo	Hawthorn fruit	12326306	1
Caelo	Hawthorn fruit	13367203	1
Caelo	Hawthorn fruit	12326307	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Hawthorn fruit	2806B110818	2
Klenk	Hawthorn fruit	2806B121203	2
Caelo	Hawthorn fruit	12326304	1
an	Hawthorn leaf with fl...	1971A130930	2
Bahnhof-Apotheke	Hawthorn leaf with fl...	7-121011	1
Bombastus	Hawthorn leaf with fl...	264044	1
Bombastus	Hawthorn leaf with fl...	267551	1
Bombastus	Hawthorn leaf with fl...	272881	1
Bombastus	Hawthorn leaf with fl...	267000	1
Bombastus	Hawthorn leaf with fl...	273287	1
Bombastus	Hawthorn leaf with fl...	278756	1
Caelo	Hawthorn leaf with fl...	10273512	2
Caelo	Hawthorn leaf with fl...	10273515	6
Caelo	Hawthorn leaf with fl...	11366001	1
Caelo	Hawthorn leaf with fl...	11068206	1
Caelo	Hawthorn leaf with fl...	12225104	12
Caelo	Hawthorn leaf with fl...	1222514	1
Caelo	Hawthorn leaf with fl...	12225108	7
Caelo	Hawthorn leaf with fl...	IntCh: 313082	1
Caelo	Hawthorn leaf with fl...	12225107	5
Caelo	Hawthorn leaf with fl...	13276703	3
Caelo	Hawthorn leaf with fl...	15188802	1
Caelo	Hawthorn leaf with fl...	1518802	1
Caelo	Hawthorn leaf with fl...	16025802	1
Caelo	Hawthorn leaf with fl...	2225104	1
Caelo	Hawthorn leaf with fl...	109076	1
Caelo	Hawthorn leaf with fl...	1225107	1
Caelo	Hawthorn leaf with fl...	12225207	1
Caelo	Hawthorn leaf with fl...	52467476	1
Caelo	Hawthorn leaf with fl...	1221707	1
Galke	Hawthorn leaf with fl...	21126	3
Gehe	Hawthorn leaf with fl...	1351B111207	2
Kenk / Phoenix	Hawthorn leaf with fl...	1971A130307	6
Klenk	Hawthorn leaf with fl...	1971A110620	5
Klenk	Hawthorn leaf with fl...	1971A120215	3
Klenk	Hawthorn leaf with fl...	14101301	1
Klenk	Hawthorn leaf with fl...	28101307	1
Klenk	Hawthorn leaf with fl...	20121302	1
Klenk	Hawthorn leaf with fl...	A130307	1
Klenk	Hawthorn leaf with fl...	1971a120813	2
Klenk	Hawthorn leaf with fl...	1972A120727	1
Klenk	Hawthorn leaf with fl...	1971A120813	20
Klenk	Hawthorn leaf with fl...	1971A120727	13
Klenk	Hawthorn leaf with fl...	1971a120215	1
Klenk	Hawthorn leaf with fl...	1971A120813-34103101	1
Klenk	Hawthorn leaf with fl...	1971A130307-3447	1
Klenk	Hawthorn leaf with fl...	1971A130307-35014110	1
Bombastus	Hawthorn leaf with fl...	275310	2
vedono	Hawthorn leaf with fl...	12225103	4
Bahnhof-Apotheke	Hay flower	13-121105	1
Caelo	Hay flower	11099912	1
Caelo	Hay flower	25101202	1
Caelo	Hay flower	11099914	1
Caelo	Hay flower	11099916	1
Caelo	Hay flower	11099909	1
Caelo	Hay flower	12317102	3
Caelo	Hay flower	1231702	1
Caelo	Hay flower	12317108	3
Caelo	Hay flower	12317107	14
Caelo	Hay flower	13097302	9

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Hay flower	12317110	2
Caelo	Hay flower	13099205	1
Caelo	Hay flower	14121301	1
Caelo	Hay flower	13097301	1
Caelo	Hay flower	11099902	1
Caelo	Hay flower	12317104	10
Caelo	Hay flower	3713E-01459	1
Caelo	Hay flower	3713F-01459	1
Caelo	Hay flower	12317101	8
Caelo	Hay flower	12371707	1
Galke	Hay flower	21926	1
Klenk	Hay flower	A130304	1
Klenk	Hay flower	10192103	1
Klenk	Hay flower	1400A120116	1
Nachprüfung	Hay flower	1911E01459	1
Caelo	Hay flower	11099915	1
Caelo	Heather flower, rubbed	10270516	1
Caelo	Heather flower, rubbed	13014204	5
Caelo	Heather flower, rubbed	13014206	1
Klenk	Heather flower, rubbed	13014202	1
Alliance	Heather, cut	255389	1
Bombastus	Heather, cut	278314	1
Caelo	Heather, cut	28061201	1
Caelo	Heather, cut	9291512	1
Caelo	Heather, cut	19111203	1
Caelo	Heather, cut	11011209	3
Caelo	Heather, cut	11102901	1
Caelo	Heather, cut	13367502	1
Caesar/Noweda	Heather, cut	4911I-03224	1
Nachprüfung	Heather, cut	5110A03224	1
5N Plus Lübeck GmbH/ ...	Heavy alkaline bismut...	12146908	1
Caelo	Heavy alkaline bismut...	12146902	1
Caelo	Heavy alkaline bismut...	12146911	3
Caelo	Heavy alkaline bismut...	4513M-01186	1
Caelo	Heavy alkaline bismut...	12146913	2
Caelo	Heavy alkaline bismut...	M468105	1
Caelo	Heavy alkaline bismut...	12146903	4
Caelo	Heavy alkaline bismut...	10013208	1
Caelo	Heavy alkaline bismut...	10F09-N13	1
Caelo	Heavy alkaline bismut...	10013213	1
Caelo	Heavy alkaline bismut...	11052805	1
Caelo	Heavy alkaline bismut...	11052809	1
Caesar & Loretz/ Noweda	Heavy alkaline bismut...	12145701	1
Fagron	Heavy alkaline bismut...	1309211186	1
Fagron	Heavy alkaline bismut...	12C08-N06	3
Fagron	Heavy alkaline bismut...	12D26-N03	1
Fagron	Heavy alkaline bismut...	1001311186	1
Fagron	Heavy alkaline bismut...	13C15-N05	3
Fagron	Heavy alkaline bismut...	13H28-B04-291385	1
Fagron	Heavy alkaline bismut...	11D28-N16	1
Fagron	Heavy alkaline bismut...	13B25-N02	3
Fagron	Heavy alkaline bismut...	11/13-N01	1
Merck	Heavy alkaline bismut...	75419201	1
Noweda	Heavy alkaline bismut...	13/01-N02	1
Purren Apotheke	Heavy alkaline bismut...	11H31-N06	1
Sanacorp	Heavy alkaline bismut...	12146909	2
Euro OTC	Heavy magnesium oxide	1205012-01	1
Euro OTC	Heavy magnesium oxide	1012033-01	1
Caelo	Henna powder	12122301	2
Caelo	Henna powder	12122310	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Henna powder	13262803	2
Caelo	Henna powder	12267311	1
Klenk	Henna powder	20747A111004	1
Klenk	Henna powder	2074A111004	1
Caelo	Hop strobile	13123802	9
Bombaltus	Hop strobile	274724	1
Bombastus	Hop strobile	276976	1
Bombastus	Hop strobile	271870	1
Bombastus	Hop strobile	208502	1
Caelo	Hop strobile	15061211	1
Caelo	Hop strobile	12008307	2
Caelo	Hop strobile	1451b120817	1
Caelo	Hop strobile	5021306	1
Caelo	Hop strobile	12008317	6
Caelo	Hop strobile	12380101	6
Caelo	Hop strobile	12380103	2
Caelo	Hop strobile	1451B130107	6
Caelo	Hop strobile	6091303	1
Caelo	Hop strobile	13123803	8
Caelo	Hop strobile	12221807	1
Caelo	Hop strobile	13123902	1
Caelo	Hop strobile	4111304	1
Caelo	Hop strobile	13123807	1
Caelo	Hop strobile	30121301	1
Caelo	Hop strobile	13123803	1
Caelo	Hop strobile	13123804	3
Caelo	Hop strobile	131223805	1
Caelo	Hop strobile	14068007	1
Caelo	Hop strobile	12221804	1
Caelo	Hop strobile	12008302	1
Caelo	Hop strobile	12008315	1
Caelo	Hop strobile	4756769	1
Caelo	Hop strobile	12008309	3
Caelo	Hop strobile	10240308	1
Caelo	Hop strobile	13187602	1
Caelo	Hop strobile	12008305	1
Caelo	Hop strobile	120008312	1
Caelo	Hop strobile	12221805	3
Caelo	Hop strobile	12221802	2
Caelo	Hop strobile	12092001	2
Caelo	Hop strobile	12008310	3
Caelo	Hop strobile	12008310	3
Caelo	Hop strobile	12006305	1
Caelo	Hop strobile	12008313	2
Caelo	Hop strobile	12008317	1
Caelo	Hop strobile	13123803-3505411011	1
Caelo	Hop strobile	13123804-3563412081	1
Galke	Hop strobile	20928	3
Galke	Hop strobile	20928	2
Galke	Hop strobile	23363	1
Caelo	Hop strobile	13123806	1
Klenk	Hop strobile	1451B120202	6
Klenk	Hop strobile	1451B111004	1
Klenk	Hop strobile	20071301	1
Klenk	Hop strobile	B130409	1
Klenk	Hop strobile	1451b130409	1
Klenk	Hop strobile	1451B140408	1
Klenk	Hop strobile	1450A110712	1
Klenk	Hop strobile	1451B130409	1
Klenk	Hop strobile	1451b130107	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Hop strobile	1451B130409	9
Klenk	Hop strobile	1451B-120817	1
Klenk	Hop strobile	1451B120817	7
Noweda	Hop strobile	274725	1
Caelo	Hop strobile	13123802	3
Galke	Horse chestnut flower...	2614	1
Klenk	Horse chestnut flower...	1440A110311	3
Richter	Horse chestnut flower...	s-09/09	1
Anzag ek:2,50EUR 15.09.12	Horse chestnut leaf, ...	2551B111013	7
Apotheke Bühlau	Horse chestnut leaf, ...	100416	1
Caelo	Horse chestnut leaf, ...	11063503	2
Gehe	Horse chestnut leaf, ...	2551B131024	1
Klenk	Horse chestnut leaf, ...	255100903	1
Klenk	Horse chestnut leaf, ...	N130124	2
Klenk	Horse chestnut leaf, ...	2551N130124	3
Klenk	Horse chestnut leaf, ...	2551B081223	1
Fagron	Hydrocortisone butyrate	16j21-b01	1
Fagron	Hydrocortisone butyrate	15G08-B16-314883	1
Caelo	Hydromorphone hydroch...	14210405	1
Caelo	Hydromorphone hydroch...	18316002	2
Caelo	Hydromorphone hydroch...	16123805	2
Caelo	Hydromorphone hydroch...	16273604	1
Caesar & Loretz GmbH/...	Hydromorphone hydroch...	18188402	1
Fagron	Hydromorphone hydroch...	13I27-N05	1
Fagron	Hydromorphone hydroch...	17F0-B01-337510	2
Caelo	Hydromorphone hydroch...	15393605	1
Fagron	Hydromorphone hydroch...	15L08-B08-316877	1
Fagron	Hydromorphone hydroch...	12G05-N02	1
Caelo	Hyssop herb, cut	11374304	1
Caelo	Hyssop herb, cut	13143902	1
Caesar & Loretz/ Noweda	Hyssop herb, cut	11374301	1
Galke	Hyssop herb, cut	20939	1
Phönix	Hyssop herb, cut	11374306	1
Sanacorp	Hyssop herb, cut	11374303	2
Sanacorp	Hyssop herb, cut	13336101	7
-	Iceland moss, cut	4711E-01774	1
Anzag ek: 15,60 20.07...	Iceland moss, cut	11101605	1
Bombastus	Iceland moss, cut	13357802	1
Caelo	Iceland moss, cut	13350805	4
Caelo	Iceland moss, cut	11101601	1
Caelo	Iceland moss, cut	11101607	8
Caelo	Iceland moss, cut	4912E-01774	1
Caelo	Iceland moss, cut	12187002	1
Caelo	Iceland moss, cut	11053916	1
Caelo	Iceland moss, cut	12187103	1
Caelo	Iceland moss, cut	12187106	3
Caelo	Iceland moss, cut	12187109	4
Caelo	Iceland moss, cut	12187107	1
Caelo	Iceland moss, cut	13350803	4
Caelo	Iceland moss, cut	12382806	1
Caelo	Iceland moss, cut	13350807	4
Caelo	Iceland moss, cut	14304402	1
Caelo	Iceland moss, cut	14304401	1
Caelo	Iceland moss, cut	14304407	2
Caelo	Iceland moss, cut	15297601	1
Caelo	Iceland moss, cut	15297606	1
Caelo	Iceland moss, cut	18078207	1
Caelo	Iceland moss, cut	12197002	1
Caelo	Iceland moss, cut	12187102	20
Caelo	Iceland moss, cut	12187108	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Iceland moss, cut	15297605	4
Caelo	Iceland moss, cut	14304403	2
Caelo	Iceland moss, cut	11053911	1
Caelo	Iceland moss, cut	1287102	1
Caelo	Iceland moss, cut	14304409	6
Caelo	Iceland moss, cut	9052804	2
Caelo	Iceland moss, cut	15297603	1
caesar&loretz,Phönix	Iceland moss, cut	14304404	3
Galke	Iceland moss, cut	12369	1
Gehe	Iceland moss, cut	11101603	1
Gehe	Iceland moss, cut	11053915	1
Gehe	Iceland moss, cut	18079703	1
Klenk	Iceland moss, cut	5191N110609	1
Klenk	Iceland moss, cut	5191A140828	2
noweda	Iceland moss, cut		1
Phönix	Iceland moss, cut	12187104	3
Fagron	Indigo carmine	12K06-N11	1
Fagron	Indigo carmine	12A20-N067-16	1
Fagron	Indigo carmine	5132316	1
Fagron	Indigo carmine	13K12-N01	1
Fagron	Indigo carmine	11F09-N06	1
Caelo	Iron (III) sulfate hy...	12175908	1
Caelo	Iron (III) sulfate hy...	1512210007	1
Caelo	Iron (III) sulfate hy...	10354412	1
Caelo	Iron (III) sulfate hy...	12175906	1
Caelo	Iron (III) sulfate hy...	10354404	1
Caelo	Iron (III) sulfate hy...	10354415	1
Anzag	Ispaghula seed	11185818	1
Caelo	Ispaghula seed	4121201	1
Caelo	Ispaghula seed	4121202	1
Caelo	Ispaghula seed	9011302	1
Caelo	Ispaghula seed	10011303	1
Caelo	Ispaghula seed	413E-03369	1
Caelo	Ispaghula seed	3051302	1
Caelo	Ispaghula seed	19061308	1
Caelo	Ispaghula seed	18071301	1
Caelo	Ispaghula seed	5091319	1
Caelo	Ispaghula seed	30101302	1
Caelo	Ispaghula seed	16121302	1
Caelo	Ispaghula seed	26011401	1
Caelo	Ispaghula seed	14031408	1
Caelo	Ispaghula seed	11061405	1
Caelo	Ispaghula seed	4114001	1
Caelo	Ispaghula seed	12276527	1
Caelo	Ispaghula seed	23011505	1
Caelo	Ispaghula seed	14246602	3
Caelo	Ispaghula seed	142660	1
Caelo	Ispaghula seed	29061510	1
Caelo	Ispaghula seed	15081503	1
Caelo	Ispaghula seed	15121901	1
Caelo	Ispaghula seed	8041702	1
Caelo	Ispaghula seed	28111703	1
Caelo	Ispaghula seed	18061804	1
Caelo	Ispaghula seed	15249315	1
Caelo	Ispaghula seed	12252709	1
Caelo	Ispaghula seed	1227506	1
Caelo	Ispaghula seed	12276511	1
Caelo	Ispaghula seed	15249319	2
Caelo	Ispaghula seed	12276501	2
Caesar/Noweda	Ispaghula seed	12276503	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar/Noweda	Ispaghula seed	12276509	3
Caesar/Noweda	Ispaghula seed	12276516	1
Cealo	Ispaghula seed	12276502	4
Klenk	Ispaghula seed	7560A130710	1
Klenk	Ispaghula seed	7560A120828	7
Klenk	Ispaghula seed	20071302	1
Klenk	Ispaghula seed	7560A130418	2
Klenk	Ispaghula seed	7560A160229	1
Klenk	Ispaghula seed	7560A140203	1
Klenk	Ispaghula seed	7560A150420	3
Caelo	Ispaghula seed	11185811	2
Caelo	Ivy leaf, cut	23121303	1
Caelo	Ivy leaf, cut	23121305	1
Caelo	Ivy leaf, cut	8061205	1
Caelo	Ivy leaf, cut	11101205	1
Caelo	Ivy leaf, cut	15101203	1
Caelo	Ivy leaf, cut	20111211	1
Caelo	Ivy leaf, cut	4011301	1
Caelo	Ivy leaf, cut	11229505	5
Caelo	Ivy leaf, cut	2031301	1
Caelo	Ivy leaf, cut	12225603	2
Caelo	Ivy leaf, cut	11041303	1
Caelo	Ivy leaf, cut	12225602	1
Caelo	Ivy leaf, cut	27111301	1
Caelo	Ivy leaf, cut	10011401	1
Caesar & Loretz/ Noweda	Ivy leaf, cut	12225606	5
Gehe	Ivy leaf, cut	2061B080402	1
Klenk	Ivy leaf, cut	B130118	1
Phönix	Ivy leaf, cut	11101102	1
Caelo	Ivy leaf, cut	12225605	5
Caelo	Jasmine flower	12143203	3
Klenk	Jasmine flower	1460A110505	1
Phönix	Jasmine flower	12143206	1
Caelo	Java tea, cut	20111207	1
Caelo	Java tea, cut	31121203	1
Caelo	Java tea, cut	2221B121112	16
Caelo	Java tea, cut	12225702	1
Caelo	Java tea, cut	21061304	1
Caelo	Java tea, cut	28101305	1
Caelo	Java tea, cut	12225704	3
Caelo	Java tea, cut	13258804	3
Caelo	Java tea, cut	2221A110825	2
Caelo	Java tea, cut	11212901	1
Klenk	Java tea, cut	2221B12112	1
Klenk	Java tea, cut	2221B110718	6
Klenk	Java tea, cut	B110718	1
Klenk	Java tea, cut	B121112	3
Klenk	Java tea, cut	17121304	1
Caelo	Java tea, cut	13258802	2
VDL	Java tea, cut	2221B101213	1
Aurica / 11	Juniper	521301390	1
Aurica/Phönix	Juniper	521006043	1
Caelo	Juniper	12028610	1
Caelo	Juniper	12330505	2
Klenk	Juniper	2890A101201	5
Klenk	Juniper	2890A120709	13
Klenk	Juniper	A120709	3
Klenk	Juniper	2890a101201	3
Klenk	Juniper	2890a120709	1
Klenk	Juniper	2890A130513	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Phoenix	Juniper		1
Phönix	Juniper	13020903	1
Sanacorp	Juniper	12330509	1
Caelo	Juniper, pounded	13031302	1
Caelo	Juniper, pounded	14149502	1
Caelo	Juniper, pounded	13367302	1
Gehe	Juniper, pounded	13020903	1
Gehe am 27.03.2014	Juniper, pounded	2890A130513	1
Klenk	Juniper, pounded	2896B121016	7
Caelo	Kaolin, heavy	11041610	1
Caelo	Kaolin, heavy	11350106	2
Caelo	Kaolin, heavy	11350115	1
Caelo	Kaolin, heavy	10176518	1
Caelo	Kaolin, heavy	11350124	4
Caelo	Kaolin, heavy	11350107	1
Caelo	Kaolin, heavy	82043269	1
Caelo	Kaolin, heavy	13041803	1
Caelo	Kaolin, heavy	13041835	2
Caelo	Kaolin, heavy	13041801	2
Caelo	Kaolin, heavy	13041834	1
Caelo	Kaolin, heavy	11350107	5
Caelo	Kaolin, heavy	13041803	1
Caelo	Kaolin, heavy	11350125	4
Caelo	Kaolin, heavy	13041835	1
Caelo	Kaolin, heavy	63033516	1
Klenk	Kaolin, heavy	424A100819	2
Klenk	Kaolin, heavy	45131I01190	1
Klenk	Kaolin, heavy	424A130507	4
Klenk	Kaolin, heavy	424A130507	2
Caelo	Kelp, cut	11351109	1
Caelo	Kelp, cut	14071502	1
Caelo	Kelp, cut	11352209	1
Klenk	Kelp, cut	1051A110920	1
Caelo	Kelp, cut	280172	4
Sanacorp	Kelp, cut	11351105	1
Caelo	Kidney vetch, coarsel...	13104301	2
Caelo	Knotgrass, cut	4301A100126	2
Caelo	Knotgrass, cut	8111202	1
Caelo	Knotgrass, cut	12295702	3
Caelo	Knotgrass, cut	12295704	4
Caelo	Knotgrass, cut	4312M-01674	1
Caelo	Knotgrass, cut	12368904	1
Caelo	Knotgrass, cut	14079304	1
Caelo	Knotgrass, cut	12368903	1
Caelo	Knotgrass, cut	7102427	1
Caelo	Knotgrass, cut	12368906	3
Finze	Knotgrass, cut	10237202	1
Klenk	Knotgrass, cut	4301A120912	1
Klenk	Knotgrass, cut	4301A121120	3
Caelo	Knotgrass, cut	12368902	5
Caelo	Ladys bedstraw herb,...	10375707	2
Caelo	Ladys bedstraw herb,...	24101201	1
Caelo	Ladys bedstraw herb,...	11265102	9
Caelo	Ladys bedstraw herb,...	7011301	1
Caelo	Ladys bedstraw herb,...	2401311647	1
Caelo	Ladys bedstraw herb,...	22041303	1
Caelo	Ladys bedstraw herb,...	11265104	1
Caelo	Ladys bedstraw herb,...	14019202	1
Caelo	Ladys bedstraw herb,...	15029906	1
Caelo	Ladys bedstraw herb,...	11265103	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Ladys bedstraw herb,...	10375702	1
Caelo	Ladys bedstraw herb,...	12369002	3
Caelo	Ladys bedstraw herb,...	12369006	5
Caelo	Ladys bedstraw herb,...	12369007	3
Caesar&loretz,Phoenix	Ladys bedstraw herb,...	14019206	1
Caesar&loretz,Phoenix	Ladys bedstraw herb,...	14019215	1
Fagron	Ladys bedstraw herb,...	12369004	2
Galke	Ladys bedstraw herb,...	21942	2
Caelo	Ladys bedstraw herb,...	12369001	3
Klenk	Ladys bedstraw herb,...	3921B12030	1
Klenk	Ladys bedstraw herb,...	3921C130226	1
Caelo	Ladys bedstraw herb,...	11265106	3
Sanacorp	Ladys bedstraw herb,...	11265109	1
Sanacorp	Ladys bedstraw herb,...	12369003	8
Caelo	Lapacho wood, cut	19061301	1
Caelo	Lapacho wood, cut	13298308	1
Caelo	Lapacho wood, cut	11154506	1
Caelo	Lapacho wood, cut	2x11154506	1
Caelo	Lapacho wood, cut	12239303	2
Caelo	Lapacho wood, cut	12239305	8
Kenk / Phoenix	Lapacho wood, cut	5161A110204	1
Klenk	Lapacho wood, cut	13298302	1
Caelo	Lapacho wood, cut	13298305	1
Caelo	Large waybread herb, ...	14125907	1
Caelo	Large waybread herb, ...	10349610	1
Caelo	Large waybread herb, ...	12374104	7
Caelo	Large waybread herb, ...	123741004	1
Caelo	Large waybread herb, ...	10349614	1
Caelo	Large waybread herb, ...	12374106	2
Caelo	Large waybread herb, ...	13232401	1
Caelo	Large waybread herb, ...	13232404	1
Caelo	Large waybread herb, ...	10349603	2
Caelo	Large waybread herb, ...	10349605	1
Caelo	Large waybread herb, ...	12374101	4
Caelo	Large waybread herb, ...	9311208	1
Klenk	Large waybread herb, ...	4281N110404	1
Klenk	Large waybread herb, ...	N111121	1
Klenk	Large waybread herb, ...	4281N111121	5
Caelo	Laurel leaf	12299106	3
Caelo	Laurel leaf	12299101	1
Klenk	Laurel leaf	B110809	1
Klenk	Laurel leaf, cut	B110809	2
Anzag	Lavender flower	1488A12803	1
Bombastus	Lavender flower	268832	1
Bombastus	Lavender flower	274469	1
Bombastus	Lavender flower	279213	1
Caelo	Lavender flower	11054104	2
Caelo	Lavender flower	15061201	1
Caelo	Lavender flower	15061209	1
Caelo	Lavender flower	11327903	6
Caelo	Lavender flower	11327905	2
Caelo	Lavender flower	27091202	1
Caelo	Lavender flower	12088002	4
Caelo	Lavender flower	12088003	8
Caelo	Lavender flower	12031302	1
Caelo	Lavender flower	12088005	3
Caelo	Lavender flower	19071303	1
Caelo	Lavender flower	6091304	1
Caelo	Lavender flower	13185002	1
Caelo	Lavender flower	13159601	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lavender flower	13336008	1
Caelo	Lavender flower	13387204	1
Caelo	Lavender flower	11054107	1
Caelo	Lavender flower	11054106	2
Caelo	Lavender flower	12088006	3
Caelo	Lavender flower	1318501	1
Caelo	Lavender flower	13185001-3389311070	1
Caelo	Lavender flower	13185001-3415310152	1
Caelo	Lavender flower	13185006	1
Caelo	Lavender flower	13185001	28
Fagron	Lavender flower	1489A120919	6
Galke	Lavender flower	21416	2
Hepart AG	Lavender flower	A130214	4
Herbasinica	Lavender flower	1488A130830	1
Caelo	Lavender flower	13185003	10
Klenk	Lavender flower	1489A1203	1
Klenk	Lavender flower	1488A111201	2
Klenk	Lavender flower	1488A120803	3
Klenk	Lavender flower	1488B130604	5
Klenk	Lavender flower	313U-01462	1
Klenk	Lavender flower	1489A100125	1
Klenk	Lavender flower	1489A120103	19
Klenk	Lavender flower	1489A130214	16
Klenk	Lavender flower	1488B130111	2
Caelo	Lemon grass, cut	13149703	1
Caelo	Lemon grass, cut	13341301	1
Caelo	Lemon grass, cut	11301509	2
Caelo	Lemon grass, cut	11301501	1
Klenk	Lemon grass, cut	7721A130708	1
Klenk	Lemon grass, cut	A120906	1
Klenk	Lemon grass, cut	A130907	1
Klenk	Lemon grass, cut	7721A120906	1
Caelo	Lemon grass, cut	13149701	4
Caelo	Lemon grass, cut	11301503	1
Wolf	Lemon grass, cut	B654	1
Caelo	Lemon peel, cut	12217402	1
Caelo	Lemon peel, cut	12217401	1
Caelo	Lemon peel, cut	12217404	1
Galke	Lemon peel, cut	22975	1
Klenk	Lemon peel, cut	621A130221	1
Klenk	Lemon peel, cut	621A091016	1
Klenk	Lemon peel, cut	B130521	1
Klenk	Lemon peel, cut	A130221	3
Caelo	Lemon verbena leaf, cut	13037702	1
Caelo	Lemon verbena leaf, cut	12137505	1
Caelo	Lemon verbena leaf, cut	12137507	3
Caelo	Lemon verbena leaf, cut	10018208	1
Klenk	Lemon verbena leaf, cut	2411B110408	2
Wolf	Lemon verbena leaf, cut	E-587	1
Wolf	Lemon verbena leaf, cut	B-312	1
Wolf	Lemon verbena leaf, cut	23635	1
Caelo	Lime flower, cut	11086305	7
Bahnhof-Apotheke	Lime flower, cut	7-121011	1
Bombastus	Lime flower, cut	275129	2
Bombastus	Lime flower, cut	280678	3
Caelo	Lime flower, cut	9206604	1
Caelo	Lime flower, cut	10273608	2
Caelo	Lime flower, cut	11086307	3
Caelo	Lime flower, cut	272958	7
Caelo	Lime flower, cut	12170703	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lime flower, cut	1210702	1
Caelo	Lime flower, cut	10273606	1
Caelo	Lime flower, cut	12170702	2
Caelo	Lime flower, cut	28031302	1
Caelo	Lime flower, cut	Int.Ch:210140	1
Caelo	Lime flower, cut	12170701	1
Caelo	Lime flower, cut	15111301	1
Caelo	Lime flower, cut	13337403	5
Caelo	Lime flower, cut	13101708	1
Caelo	Lime flower, cut	15068302	1
Caelo	Lime flower, cut	268709	2
Caelo	Lime flower, cut	13101701	7
Caelo	Lime flower, cut	12170702-3355319071	1
Caelo	Lime flower, cut	13337403-348012102	1
Caelo	Lime flower, cut	13101702	8
galke,	Lime flower, cut	2098	1
Klenk	Lime flower, cut	1611B120827	11
Klenk	Lime flower, cut	1611B130905	5
Klenk	Lime flower, cut	1611B110421	2
Klenk	Lime flower, cut	Pr.Nr.4411A-01474	1
Klenk	Lime flower, cut	B130307	2
Klenk	Lime flower, cut	1611B1010004	1
Klenk	Lime flower, cut	B130905	4
Klenk	Lime flower, cut	1611B131220	1
Klenk	Lime flower, cut	1611B121105	4
Klenk	Lime flower, cut	1611a121120	2
Klenk	Lime flower, cut	1611A121120	7
Klenk	Lime flower, cut	1611B111011	5
Klenk	Lime flower, cut	1611B130307	4
Phönix	Lime flower, cut	2090413	1
Phönix	Lime flower, cut	1611A12120	1
Sanacorp	Lime flower, cut	264045	1
Wolf	Lime flower, cut	B449	1
Wolf	Lime flower, cut	22094	1
Caelo	Lime leaf, cut	1611A121120	1
Klenk	Lime leaf, cut	2471B120502	1
Akazie	Linseed	20.09.2015	2
Anzag	Linseed	12137105	1
Bombastus	Linseed	1610	1
Bombastus	Linseed	269500	1
Bombastus	Linseed	278457	6
Bombastus	Linseed	274032	1
Bombastus	Linseed	282734	3
Bombastus	Linseed	295376	1
Caelo	Linseed	15061201	1
Caelo	Linseed	12092102	4
Caelo	Linseed	11365508	1
Caelo	Linseed	11365507	1
Caelo	Linseed	12092103	3
Caelo	Linseed	12321601	1
Caelo	Linseed	12092104	2
Caelo	Linseed	28051303	1
Caelo	Linseed	12321602	4
Caelo	Linseed	12321604	2
Caelo	Linseed	11199006	1
Caelo	Linseed	1232006	1
Caelo	Linseed	12382006	3
Caelo	Linseed	12321607	1
Caelo	Linseed	18111302	1
Caelo	Linseed	12321606	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Linseed	13262702	1
Caelo	Linseed	13296702	3
Caelo	Linseed	13262703	3
Caelo	Linseed	28051403	1
Caelo	Linseed	1326703	2
Caelo	Linseed	7370A131104	1
Caelo	Linseed	13140305	1
Caelo	Linseed	13412804	1
Caelo	Linseed	13262704	2
Caelo	Linseed	15053702	1
Caelo	Linseed	13296707	1
Caelo	Linseed	15006602	1
Caelo	Linseed	15006005	1
Caelo	Linseed	15006605	1
Caelo	Linseed	15321902	1
Caelo	Linseed	21081703	1
Caelo	Linseed	12382002	2
Caelo	Linseed	16355404	1
Caelo	Linseed	18007801	2
Caelo	Linseed	18145601	1
Caelo	Linseed	13296705	5
Caelo	Linseed	16040002	1
Caelo	Linseed	17067204	1
Caelo	Linseed	16040005	1
Caelo	Linseed	12186901	2
Caelo	Linseed	16040001	1
Caelo	Linseed	16011403	3
Caelo	Linseed	15006601	2
Caelo	Linseed	15006607	1
Caelo	Linseed	16355401	2
Caelo	Linseed	4713U02240	1
Caelo	Linseed	7307A170619	2
Caelo	Linseed	3615A-02240	1
Caelo	Linseed	11199003	1
Caelo	Linseed	7307A141201	2
Fiebig	Linseed	16011405	4
Caelo	Linseed	16355402	4
Finze	Linseed	3607E-02240	1
Gehe	Linseed	18145603	1
Gehe	Linseed	18145605	1
Hedinger	Linseed	16011402	1
Heinrich Kle/Sanacor	Linseed	7307A170111	2
Klenk	Linseed	1910212240	1
Klenk	Linseed	903312240	1
Klenk	Linseed	7300A111107	4
Klenk	Linseed	7308A111107	3
Klenk	Linseed	7300A130110	7
Klenk	Linseed	1913Q-02240	1
Klenk	Linseed	A130110	1
Klenk	Linseed	7307A130722	5
Klenk	Linseed	7307A-130722	1
Klenk	Linseed	7300A140526	1
Klenk	Linseed	7308A150710	2
Klenk	Linseed	7300A170306	6
Klenk	Linseed	7300A180523	2
Klenk	Linseed	7300A170306-1	1
Klenk	Linseed	7300A141201	6
Klenk	Linseed	7308A150414	2
Klenk	Linseed	7307A130124	1
Klenk	Linseed	7307A150710	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Linseed	7307a131104	1
Klenk	Linseed	7307A160414	1
Klenk	Linseed	7307A140526	3
Klenk	Linseed	7308A130110	4
Klenk	Linseed	2002285	1
Klenk	Linseed	7307A131104	8
Klenk	Linseed	7307A-130110	1
Klenk	Linseed	3707A140526	1
Klenk	Linseed	7500A140556	1
Klenk	Linseed	7300A130722	8
Midas	Linseed	7308A161208	1
Noweda	Linseed	7307A111107	7
Klenk	Linseed	7307a111107	1
Klenk	Linseed	7307A121212	1
Caelo	Linseed	12382004	1
Klenk	Linseed	7307A131021	1
Phonix	Linseed	13296703	3
Klenk	Linseed	7307A130110	15
Bahnhof-Apotheke	Liquorice root, peeled	17-121112	1
Bombastus	Liquorice root, peeled	268001	1
Bombastus	Liquorice root, peeled	270192	1
Caelo	Liquorice root, peeled	6381A111004	14
Caelo	Liquorice root, peeled	1135904	1
Caelo	Liquorice root, peeled	11351911	4
Caelo	Liquorice root, peeled	10011301	1
Caelo	Liquorice root, peeled	11351913	1
Caelo	Liquorice root, peeled	11351910	2
Caelo	Liquorice root, peeled	638a120806	1
Caelo	Liquorice root, peeled	13104503	3
Caelo	Liquorice root, peeled	13104504	4
Caelo	Liquorice root, peeled	18121302	1
Caelo	Liquorice root, peeled	1351911	1
Caelo	Liquorice root, peeled	13194101	5
Caesar & Loretz GmbH,...	Liquorice root, peeled	11034014	1
Galke	Liquorice root, peeled	23538	1
Gehe	Liquorice root, peeled	268835	1
Gehe	Liquorice root, peeled	270853	3
Gehe	Liquorice root, peeled	1250213	1
Caelo	Liquorice root, peeled	12227112	1
Klenk	Liquorice root, peeled	6381a111004	1
Klenk	Liquorice root, peeled	6381A121126	27
Klenk	Liquorice root, peeled	6381A130426	21
Klenk	Liquorice root, peeled	A130426	1
Klenk	Liquorice root, peeled	A130820	3
Klenk	Liquorice root, peeled	6381A130820	4
Klenk	Liquorice root, peeled	6381A140109	2
Klenk	Liquorice root, peeled	6381A130425	1
Klenk	Liquorice root, peeled	6381A110531	2
Klenk	Liquorice root, peeled	638A130820	1
Klenk	Liquorice root, peeled	6381a121126	1
Noweda	Liquorice root, peeled	70226/1	1
Klenk	Liquorice root, peeled	6381A120806	3
Phoenix	Liquorice root, peeled	6381A120611	12
Sanacorp	Liquorice root, peeled	11351906	3
Caelo	Liquorice root, peeled	277004	1
Caelo	Liquorice root, peeled	11351905	3
aurica/phoenix	Liquorice root, natur...	521206925	1
Bombastus	Liquorice root, natur...	2901312151	1
Bombastus	Liquorice root, natur...	903312151	1
Bombastus	Liquorice root, natur...	279409	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Liquorice root, natur...	5091305	1
Bombastus	Liquorice root, natur...	285185	2
Bombastus	Liquorice root, natur...	286584	1
Bombastus	Liquorice root, natur...	278377	3
Bombastus	Liquorice root, natur...	274921	3
Bombastus	Liquorice root, natur...	3713Q2151	1
Caelo	Liquorice root, natur...	13037904	1
Caelo	Liquorice root, natur...	10110912	1
Caelo	Liquorice root, natur...	12267103	1
Caelo	Liquorice root, natur...	13037902	1
Caelo	Liquorice root, natur...		1
Caelo	Liquorice root, natur...	12267104	2
Gehe	Liquorice root, natur...	277004	2
Gehe	Liquorice root, natur...	283316	1
Gehe	Liquorice root, natur...	284243	2
Klenk	Liquorice root, natur...	6391A080905	4
Klenk	Liquorice root, natur...	6391A110421	4
Klenk	Liquorice root, natur...	6390A101020	1
PHOENIX am 27.12.2013	Liquorice root, natur...	281844	1
Bombastus	Liquorice root, natur...	276468	6
Phönix	Liquorice root, natur...	276425	1
Bombastus	Lovage root, cut	273001	1
Caelo	Lovage root, cut	11181609	3
Caelo	Lovage root, cut	12189001	1
Caelo	Lovage root, cut	11181611	3
Caelo	Lovage root, cut	4312M-02150	1
Caelo	Lovage root, cut	12169007	1
Caelo	Lovage root, cut	12169009	1
Caelo	Lovage root, cut	12169012	1
Caelo	Lovage root, cut	13385005	1
Caelo	Lovage root, cut	12189002	1
Caelo	Lovage root, cut	107063	1
Caelo	Lovage root, cut	12169008	4
Caelo	Lovage root, cut	12169006	3
Caelo	Lovage root, cut	12169002	2
Caelo	Lovage root, cut	12169010	2
Klenk	Lovage root, cut	6371A080508	1
Klenk	Lovage root, cut	B110228	1
Klenk	Lovage root, cut	B121029	1
Klenk	Lovage root, cut	6371B-121029	1
Klenk	Lovage root, cut	6371B121029	3
Caelo	Lungwort herb, cut	11021707	1
Caelo	Lungwort herb, cut	11134203	12
Caelo	Lungwort herb, cut	4331b111205	1
Caelo	Lungwort herb, cut	13029302	25
Caelo	Lungwort herb, cut	11134205	3
Caelo	Lungwort herb, cut	11134201	1
Caelo	Lungwort herb, cut	13029306	3
Caelo	Lungwort herb, cut	11021709	2
Caelo	Lungwort herb, cut	13355801	2
Caesar & Loretz GmbH,...	Lungwort herb, cut	13029304	5
Fagron	Lungwort herb, cut	Nachprüfung	1
Galke	Lungwort herb, cut	19511	4
Klenk	Lungwort herb, cut	4331B111205	1
Klenk	Lungwort herb, cut	4331A120813	1
Richter	Lungwort herb, cut	P195884	1
Caelo	Lungwort herb, cut	11134202	3
Caelo	Lycopodium herb, cut	11255012	2
Bahnhof-Apotheke	Lycopodium herb, cut	17-121112	1
Caelo	Lycopodium herb, cut	11255003	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Lycopodium herb, cut	9378812	1
Caelo	Lycopodium herb, cut	11255005	3
Caelo	Lycopodium herb, cut	11255008	12
Caelo	Lycopodium herb, cut	11255009	3
Caelo	Lycopodium herb, cut	11255011	5
Caelo	Lycopodium herb, cut	11255014	7
Caelo	Lycopodium herb, cut	11255010	1
Caelo	Lycopodium herb, cut	11255016	2
Caelo	Lycopodium herb, cut	11255018	1
Caelo	Lycopodium herb, cut	13101501	1
Caelo	Lycopodium herb, cut	1310502	1
Caesar/Noweda	Lycopodium herb, cut	1255008	1
Finze	Lycopodium herb, cut	9378803	1
Galke	Lycopodium herb, cut	16913	3
Klenk	Lycopodium herb, cut	4111B120220	1
Klenk	Lycopodium herb, cut	4111B110428	1
Caelo	Lycopodium herb, cut	11255017	6
Sanacorp	Lycopodium herb, cut	13101502	2
Fagron	Macrogols 6000 powder	14J17-B01	1
Fagron	Macrogols 6000 powder	12J22-N02	1
Fagron	Macrogols 6000 powder	11G14-N03	1
Fagron	Magnesium aspartate d...	17C21-B05-333111	1
Caelo	Magnesium carbonate, ...	2091303	1
Caelo	Magnesium carbonate, ...	13123505	1
Caelo	Magnesium carbonate, ...	13123502	1
Caelo	Magnesium carbonate, ...	7011404	1
Caelo	Magnesium carbonate, ...	13123504	2
Caelo	Magnesium carbonate, ...	12135404	1
Euro OTC	Magnesium carbonate, ...	1305024-01	1
Fagron	Magnesium carbonate, ...	12F20-N04	1
Euro OTC	Magnesium carbonate, ...	1211005-01	4
Anzag	Magnesium chloride he...	120802501	1
Anzag	Magnesium chloride he...	1304003-01	2
Caelo	Magnesium chloride he...	16094004	1
Caelo	Magnesium chloride he...	11345606	1
Caelo	Magnesium chloride he...	11345623	2
Caelo	Magnesium chloride he...	5210I-01828	1
Caelo	Magnesium chloride he...	12141808	1
Caelo	Magnesium chloride he...	12141806	2
Caelo	Magnesium chloride he...	12354605	4
Caelo	Magnesium chloride he...	12141814	1
Caelo	Magnesium chloride he...	1512I-01828	1
Caelo	Magnesium chloride he...	12354613	4
Caelo	Magnesium chloride he...	12354608	1
Caelo	Magnesium chloride he...	13194707	4
Caelo	Magnesium chloride he...	1.02.14	1
Caelo	Magnesium chloride he...	1304C004	2
Caelo	Magnesium chloride he...	16094014	1
Caelo	Magnesium chloride he...	17034304	1
Caelo	Magnesium chloride he...	1108024-01	1
Caelo	Magnesium chloride he...	12141803	1
Caelo	Magnesium chloride he...	12141811	2
Caelo	Magnesium chloride he...	12354615	8
Caelo	Magnesium chloride he...	12354610	2
Caelo	Magnesium chloride he...	12354606	4
Fagron	Magnesium chloride he...	1304C003-281209	1
Caelo	Magnesium chloride he...	12354609	7
Caelo	Magnesium chloride he...	12354604	4
Caelo	Magnesium chloride he...	13194721	2
Caelo	Magnesium chloride he...	12141817	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Magnesium chloride he...	12354612	7
Caelo	Magnesium chloride he...	12354618	2
Caelo	Magnesium chloride he...	11345624	1
Caelo	Magnesium chloride he...	13194706	3
Caelo	Magnesium chloride he...	13194713-3490312103	1
Caelo	Magnesium chloride he...	12141807	3
Caelo	Magnesium chloride he...	13194702	3
Caelo	Magnesium chloride he...	13194713	1
Caesar & Loretz GmbH	Magnesium chloride he...	13064223	1
Cealo	Magnesium chloride he...	112354615	1
Cealo	Magnesium chloride he...	11354615	1
Euro OTC	Magnesium chloride he...	1204017-01	1
Euro OTC	Magnesium chloride he...	1112013-01	2
Euro OTC	Magnesium chloride he...	1212013-01	3
Fagron	Magnesium chloride he...	11K17-N10	1
Fagron	Magnesium chloride he...	12H21-N02	9
Fagron	Magnesium chloride he...	12B16-N01	1
Fagron	Magnesium chloride he...	12D11-N01	1
Fagron	Magnesium chloride he...	26061305	1
Fagron	Magnesium chloride he...	1301C009-277802	4
Fagron	Magnesium chloride he...	1301C011-277803	1
Fagron	Magnesium chloride he...	1301C012-277804	1
Fagron	Magnesium chloride he...	1304c004-281210	1
Fagron	Magnesium chloride he...	1304C004-281210	1
Fagron	Magnesium chloride he...	1304C001-281211	2
Fagron	Magnesium chloride he...	13411207	1
Fagron	Magnesium chloride he...	13B14-B01-287292	1
Fagron	Magnesium chloride he...	12h21-N02	1
Fagron	Magnesium chloride he...	1301C10	3
Fagron	Magnesium chloride he...	1304C002	1
Fagron	Magnesium chloride he...	M1430	1
Fagron	Magnesium chloride he...	1301c009-277802	1
Fagron	Magnesium chloride he...	1301C10-277801	1
Fagron	Magnesium chloride he...	M1555	1
Fagron	Magnesium chloride he...	12H21-N02	1
Fagron	Magnesium chloride he...	1304C003	1
Fagron	Magnesium chloride he...	M1625	1
Phönix/Euro	Magnesium chloride he...	1208025-01	2
stumpf	Magnesium chloride he...	1301c012-277804	1
Caelo	Magnesium chloride he...	11345609	1
Caelo	Magnesium chloride he...	13194701	1
Fagron	Magnesium chloride he...	12H21-No2	1
unbekannt	Magnesium chloride he...	unbekannt	1
Anzag	Magnesium sulfate hep...	204035	1
Anzag 29.04.13 ek: 4,...	Magnesium sulfate hep...	12138518	3
Bombastus	Magnesium sulfate hep...	277424	1
Caelo	Magnesium sulfate hep...	10371111	1
Caelo	Magnesium sulfate hep...	11369526	13
Caelo	Magnesium sulfate hep...	1206019-01	5
Caelo	Magnesium sulfate hep...	10104201	1
Caelo	Magnesium sulfate hep...	11369529	1
Caelo	Magnesium sulfate hep...	11194001	1
Caelo	Magnesium sulfate hep...	11369509	1
Caelo	Magnesium sulfate hep...	90744129	1
Caelo	Magnesium sulfate hep...	12119901/2	1
Caelo	Magnesium sulfate hep...	12138521	4
Caelo	Magnesium sulfate hep...	11369252	1
Caelo	Magnesium sulfate hep...	12336914	5
Caelo	Magnesium sulfate hep...	13030104	1
Caelo	Magnesium sulfate hep...	12336926	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Magnesium sulfate hep...	12336915	3
Caelo	Magnesium sulfate hep...	13030107	1
Caelo	Magnesium sulfate hep...	13183702	2
Caelo	Magnesium sulfate hep...	6012014B	1
Caelo	Magnesium sulfate hep...	12c27-n06	1
Caelo	Magnesium sulfate hep...	1213E-01835	1
Caelo	Magnesium sulfate hep...	113695625	1
EuRho	Magnesium sulfate hep...	3512M-01835	1
EuRho	Magnesium sulfate hep...	1303008-01	5
Euro / Jenne	Magnesium sulfate hep...	1401029-01	2
Euro OTC	Magnesium sulfate hep...	130300801	1
Euro OTC	Magnesium sulfate hep...	1109023-01	2
Euro OTC	Magnesium sulfate hep...	1202017-01	6
Euro OTC	Magnesium sulfate hep...	1306015-01	1
Euro OTC	Magnesium sulfate hep...	170610	1
Fagron	Magnesium sulfate hep...	12G24-N02	1
Fagron	Magnesium sulfate hep...	12L10-N07	8
Fagron	Magnesium sulfate hep...	26251	1
Fagron	Magnesium sulfate hep...	13H05-N02	1
Fagron	Magnesium sulfate hep...	12L10-N07	1
fargon	Magnesium sulfate hep...	12E22-N02	4
Hedinger	Magnesium sulfate hep...	204036	1
Hedinger	Magnesium sulfate hep...	204037	2
Noweda / 28.10.13 EuRho	Magnesium sulfate hep...	1211022-01	4
Fagron	Magnesium sulfate hep...	31161	1
Caelo	Magnesium sulfate hep...	11369525	6
Caelo	Magnesium sulfate, dr...	11265902	1
Caelo	Magnesium sulfate, dr...	11265903	1
Caelo	Magnesium sulfate, dr...	12157202	1
Caelo	Magnesium sulfate, dr...	M-220413-2	1
Caelo	Magnesium sulfate, dr...	12157207	1
Caelo	Magnesium sulfate, dr...	12157208	1
Caelo	Magnesium sulfate, dr...	10213213	2
Caelo	Magnesium sulfate, dr...	11265908	2
Anzag	Maize style, cut	274920	1
Aurica/Phönix	Maize style, cut	520901387	1
Bahnhof-Apotheke	Maize style, cut	20-121018	1
Bombastus	Maize style, cut	282574	1
Bombastus	Maize style, cut	285912	1
Bombastus	Maize style, cut	276776	1
Bombastus	Maize style, cut	81113a	1
Bombastus	Maize style, cut	17001482	1
Bombastus	Maize style, cut	19002817	1
Caelo	Maize style, cut	10325902	2
Caelo	Maize style, cut	10325906	7
Caelo	Maize style, cut	10325904	1
Caelo	Maize style, cut	10325907	4
Caelo	Maize style, cut	10325905	1
Caelo	Maize style, cut	280363	1
Caelo	Maize style, cut	11280404	2
Caelo	Maize style, cut	13277201	1
Caelo	Maize style, cut	13277202	1
Caelo	Maize style, cut	13277207	1
Caelo	Maize style, cut	11280405	11
Caelo	Maize style, cut	13277205	1
Gehe	Maize style, cut	18041004	1
Klenk	Maize style, cut	5581A081204	1
Klenk	Maize style, cut	5581A111206	1
Klenk	Maize style, cut	A110411	1
Richter	Maize style, cut	B189316	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Sana 21.10.14 Ek 3.57	Maize style, cut	13381603	2
A.H. 27.05.13 ek: 6,75EUR	Male speedwell wort, ...	274239	1
Anzag ek: 4,88EUR 26.09...	Male speedwell wort, ...	4661C120321	10
Aurica/Phönix	Male speedwell wort, ...	520708362	1
Bahnhof-Apotheke	Male speedwell wort, ...	4-121002	1
Bombastus	Male speedwell wort, ...	274238	1
Caelo	Male speedwell wort, ...	12162503	1
Caelo	Male speedwell wort, ...	11265503	5
Caelo	Male speedwell wort, ...	11265502	1
Caelo	Male speedwell wort, ...	4661c111011	1
Caelo	Male speedwell wort, ...	3051306	1
Caelo	Male speedwell wort, ...	12162504	13
Caelo	Male speedwell wort, ...	11061305	1
Caelo	Male speedwell wort, ...	28061303	1
Caelo	Male speedwell wort, ...	3091305	1
Caelo	Male speedwell wort, ...	13166701	3
Caelo	Male speedwell wort, ...	14111303	1
Caelo	Male speedwell wort, ...	20111303	1
Caelo	Male speedwell wort, ...	1216504	1
Caelo	Male speedwell wort, ...	12162505	2
Finze	Male speedwell wort, ...	4661B080915	1
Klenk	Male speedwell wort, ...	4661A090318	1
Klenk	Male speedwell wort, ...	4661B110916	1
Klenk	Male speedwell wort, ...	4661C120802	13
Klenk	Male speedwell wort, ...	4661C130226	27
Klenk	Male speedwell wort, ...	C120321	1
Klenk	Male speedwell wort, ...	C130226	5
Klenk	Male speedwell wort, ...	4661C13026	1
Klenk	Male speedwell wort, ...	4661C131104	1
Klenk	Male speedwell wort, ...	4661C111011	13
Klenk	Male speedwell wort, ...	4661B101011	1
Klenk	Male speedwell wort, ...	4661C130226-32743106	1
Klenk	Male speedwell wort, ...	4661c130226-34343111	1
Klenk	Male speedwell wort, ...	4661C2004	1
Klenk	Male speedwell wort, ...	4661C-111011	1
Klenk	Male speedwell wort, ...	4661B110121	2
Klenk	Male speedwell wort, ...	6661C130226	1
Klenk	Male speedwell wort, ...	4661c120802	1
Klenk	Male speedwell wort, ...	4661c120321	1
Phönix	Male speedwell wort, ...	13089201	4
Bombastus	Mallow flower, cut	273803	1
Bombastus	Mallow flower, cut	13267304	1
Caelo	Mallow flower, cut	20061201	1
Caelo	Mallow flower, cut	10357902	1
Caelo	Mallow flower, cut	11040106	4
Caelo	Mallow flower, cut	8121202	1
Caelo	Mallow flower, cut	27021301	1
Caelo	Mallow flower, cut	12187405	4
Caelo	Mallow flower, cut	12187404	4
Caelo	Mallow flower, cut	12187501	6
Caelo	Mallow flower, cut	12187502	1
Caelo	Mallow flower, cut	13040402	1
Caelo	Mallow flower, cut	18111303	1
Caelo	Mallow flower, cut	13267303	2
Caelo	Mallow flower, cut	13267302	1
Caelo	Mallow flower, cut	13351309	1
Caelo	Mallow flower, cut	13351307	1
Caelo	Mallow flower, cut	10357904	1
Caelo	Mallow flower, cut	13351301	2
Caelo	Mallow flower, cut	13351303	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Mallow flower, cut	9311104	1
Caelo	Mallow flower, cut	13267301-3409310112	1
Caelo	Mallow flower, cut	12187501-3414310132	1
Caesar & Loretz GmbH,...	Mallow flower, cut	12187402	8
Caesar & Loretz GmbH,...	Mallow flower, cut	13267301	5
Galke	Mallow flower, cut	21119	1
Gehe	Mallow flower, cut	1501B110207	1
Gehe	Mallow flower, cut	1501B120508	6
Klenk	Mallow flower, cut	10357908	2
Caelo	Mallow flower, cut	12187505	3
Klenk	Mallow flower, cut	1910211464	1
Klenk	Mallow flower, cut	1501B120427	10
Klenk	Mallow flower, cut	1501B111215	1
Klenk	Mallow flower, cut	1501B-120427	1
Klenk	Mallow flower, cut	B120427	1
Klenk	Mallow flower, cut	B130829	3
Klenk	Mallow flower, cut	1501b111215	1
Klenk	Mallow flower, cut	1501B130829	3
Klenk	Mallow flower, cut	150B111215	1
Klenk	Mallow flower, cut	1501B100408	1
Nachprüfung 29.10.12	Mallow flower, cut	C1316	1
Klenk	Mallow flower, cut	1501b110207	1
Caelo	Mallow leaf, cut	28061203	1
Caelo	Mallow leaf, cut	2131B120529	3
Caelo	Mallow leaf, cut	12310001	3
Caelo	Mallow leaf, cut	12310004	4
Caelo	Mallow leaf, cut	12310009	2
Caelo	Mallow leaf, cut	12310008	1
Caelo	Mallow leaf, cut	20111302	1
Caelo	Mallow leaf, cut	14073902	1
Caelo	Mallow leaf, cut	13174213	1
Caelo	Mallow leaf, cut	12153403	1
Caelo	Mallow leaf, cut	10290515	1
Caelo	Mallow leaf, cut	10290502	1
Caelo	Mallow leaf, cut	13174207	1
Galke	Mallow leaf, cut	17133	1
Galke	Mallow leaf, cut	21454	1
Galke	Mallow leaf, cut	21445	1
Gehe	Mallow leaf, cut	2131B110420	2
Gehe	Mallow leaf, cut	10290512	1
Klenk	Mallow leaf, cut	2131B10529	1
Klenk	Mallow leaf, cut	2131B130225	4
Klenk	Mallow leaf, cut	B130225	1
Sanacorp	Mallow leaf, cut	278925	1
Caelo	Mallow leaf, cut	13174217	1
Caelo	Mallow leaf, cut	12310006	1
HBK Gesundheit	Maltodextrin	1143	3
HBK Gesundheit	Maltodextrin	2343	1
Anzag ek:8.77EUR 30.08.12	Manna, cut	11308904	2
Caelo	Manna, cut	11308901	2
Caelo	Manna, cut	11308909	2
Caelo	Manna, cut	25111301	1
Caelo	Manna, cut	11041401	1
Caelo	Manna, cut	11061404	1
Caelo	Manna, cut	25071403	1
Caelo	Manna, cut	28101404	1
Caelo	Manna, cut	13041712	1
Caelo	Manna, cut	15219010	3
Caelo	Manna, cut	15111738	1
Caelo	Manna, cut	11308907	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Manna, cut	13127003	5
Caelo	Manna, cut	11308911	2
Caelo	Manna, cut	15219005	1
Caelo	Manna, cut	14001303	3
Caelo	Manna, cut	14001310	3
Caelo	Manna, cut	15219003	3
Caelo	Manna, cut	15219008	3
Klenk	Manna, cut	5221A110817	1
Klenk	Manna, cut	5221A140210	4
Klenk	Manna, cut	5221A150107	2
Caelo	Manna, cut	15219012	1
Klenk	Manna, cut	5221A120509	10
Caelo	Manna, cut	15219009	1
Caelo	Manna, powdered	11308802	2
Caelo	Manna, powdered	11003611	1
Caelo	Manna, powdered	11071311	1
Caelo	Manna, powdered	15101306	1
Caelo	Manna, powdered	15101312	1
Caelo	Manna, powdered	11308807	1
Caelo	Manna, powdered	14001402	1
Caelo	Manna, powdered	14001408	1
Galke	Manna, powdered	20669	1
Galke	Manna, powdered	19784	1
Noweda	Manna, powdered	11170102	1
Bombastus	Marian thistle fruit	296535	1
Bombastus	Marian thistle fruit	296193	1
Bombastus	Marian thistle fruit	299483	1
Bombastus	Marian thistle fruit	269499	1
Bombastus	Marian thistle fruit	280304	1
Bombastus	Marian thistle fruit	278379	1
Bombastus	Marian thistle fruit	282283	1
Bombastus	Marian thistle fruit	282034	2
Bombastus	Marian thistle fruit	279405	3
Bombastus	Marian thistle fruit	277720	3
Bombastus	Marian thistle fruit	278378	1
Bombastus	Marian thistle fruit	284420	1
Bombastus	Marian thistle fruit	13122013a	1
Caelo	Marian thistle fruit	12189116	2
Caelo	Marian thistle fruit	10270613	1
Caelo	Marian thistle fruit	11126702	9
Caelo	Marian thistle fruit	10270614	2
Caelo	Marian thistle fruit	27111203	1
Caelo	Marian thistle fruit	1126703	1
Caelo	Marian thistle fruit	11126701	1
Caelo	Marian thistle fruit	1126705	1
Caelo	Marian thistle fruit	11126705	1
Caelo	Marian thistle fruit	12189106	4
Caelo	Marian thistle fruit	12189104	2
Caelo	Marian thistle fruit	12189105	1
Caelo	Marian thistle fruit	12189109	2
Caelo	Marian thistle fruit	12189113	6
Caelo	Marian thistle fruit	12189111	3
Caelo	Marian thistle fruit	12189115	2
Caelo	Marian thistle fruit	18111301	1
Caelo	Marian thistle fruit	13326202	3
Caelo	Marian thistle fruit	15409204	2
Caelo	Marian thistle fruit	12198107	1
Caelo	Marian thistle fruit	12189107	2
Caelo	Marian thistle fruit	12189108	4
Caelo	Marian thistle fruit	11126703	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Marian thistle fruit	1289112	1
ebert u.jacobi	Marian thistle fruit	287527	1
Galke	Marian thistle fruit	22187	4
Klenk	Marian thistle fruit	7180A090929	1
Klenk	Marian thistle fruit	7180A120725	1
Klenk	Marian thistle fruit	A120725	1
Klenk	Marian thistle fruit	7180A130219	1
Klenk	Marian thistle fruit	7180A132019	1
Klenk	Marian thistle fruit	7180A110209	2
Caelo	Marian thistle fruit	12189112	5
Caelo	Marian thistle herb, ...	10365604	4
Caelo	Marian thistle herb, ...	10315909	1
Caelo	Marian thistle herb, ...	10315911	4
Caelo	Marian thistle herb, ...	10315907	1
Caelo	Marian thistle herb, ...	17121204	1
Caelo	Marian thistle herb, ...	10365601	4
Caelo	Marian thistle herb, ...	1035911	1
Caelo	Marian thistle herb, ...	18041303	1
Caelo	Marian thistle herb, ...	intch:318080	1
Caelo	Marian thistle herb, ...	13130703	2
Caelo	Marian thistle herb, ...	1313702	1
Caelo	Marian thistle herb, ...	30101306	1
Caelo	Marian thistle herb, ...	13130701	2
Caelo	Marian thistle herb, ...	13130704	5
Caelo	Marian thistle herb, ...	10365605	1
Caelo	Marian thistle herb, ...	62607127	1
Caelo	Marian thistle herb, ...	13130701-3492411030	1
Caelo	Marian thistle herb, ...	13386703-3543411013	1
Caelo	Marian thistle herb, ...	13130702	3
Euro OTC	Marian thistle herb, ...	3701A-111207	1
Gehe	Marian thistle herb, ...	10365602	2
Klenk	Marian thistle herb, ...	3701B130318	5
Klenk	Marian thistle herb, ...	11041310	1
Klenk	Marian thistle herb, ...	3701B111117	1
Klenk	Marian thistle herb, ...	B110728	1
Klenk	Marian thistle herb, ...	3701a111207	1
Klenk	Marian thistle herb, ...	2011402	1
Klenk	Marian thistle herb, ...	3701A100916	2
Klenk	Marian thistle herb, ...	913E-01627	1
Klenk	Marian thistle herb, ...	3701A111207	11
Klenk	Marian thistle herb, ...	3701B120717	3
Caelo	Marjoram herb, rubbed	12168901	3
Caelo	Marjoram herb, rubbed	11212711	3
Caelo	Marjoram herb, rubbed	12168903	10
Caelo	Marjoram herb, rubbed	12168905	2
Caelo	Marjoram herb, rubbed	12168904	1
Caelo	Marjoram herb, rubbed	12168908	6
Caelo	Marjoram herb, rubbed	6051302	1
Caelo	Marjoram herb, rubbed	12168907	3
Caelo	Marjoram herb, rubbed	12168912	1
Caelo	Marjoram herb, rubbed	27011402	1
Caelo	Marjoram herb, rubbed	11212707	1
Caelo	Marjoram herb, rubbed	12168906	1
Caelo	Marjoram herb, rubbed	13113304	3
Caelo	Marjoram herb, rubbed	12168909	6
Caelo	Marjoram herb, rubbed	13113303	3
Caelo	Marjoram herb, rubbed	12168902	1
Caelo	Marjoram herb, rubbed	12168910	8
Caelo	Marjoram herb, rubbed	9292602	1
Caesar&lorenz,Phoenix	Marjoram herb, rubbed	14181005	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Galke	Marjoram herb, rubbed	22401	1
Galke	Marjoram herb, rubbed	23241	1
Klenk	Marjoram herb, rubbed	4881A101025	15
Klenk	Marjoram herb, rubbed	A101025	2
Klenk	Marjoram herb, rubbed	4881A1311105	1
Klenk	Marjoram herb, rubbed	4881a101025	1
Klenk	Marjoram herb, rubbed	12345678	1
Noweda	Marjoram herb, rubbed	4881A100929	3
Wolf	Marjoram herb, rubbed	163516	1
Wolf	Marjoram herb, rubbed	B163516	6
Wolf	Marjoram herb, rubbed	P232243	9
Caelo	Marrubium vulgare her...	1153803	1
Caelo	Marrubium vulgare her...	12231604	4
Caelo	Marrubium vulgare her...	313091	1
Caelo	Marrubium vulgare her...	13289109	1
Caelo	Marrubium vulgare her...	11253802	1
Caelo	Marrubium vulgare her...	12231603	1
Caelo	Marrubium vulgare her...	12231601	4
Caelo	Marrubium vulgare her...	11253803	1
Caelo	Marrubium vulgare her...	12231605	4
Klenk	Marrubium vulgare her...	4141A130110	1
Klenk	Marrubium vulgare her...	13289102	1
Noweda	Marrubium vulgare her...	4141A080513	1
Caelo	Marshmallow leaf, cut	12328202	3
Caelo	Marshmallow leaf, cut	12328206	3
Caelo	Marshmallow leaf, cut	13199604	4
Caelo	Marshmallow leaf, cut	12328207	2
Bombastus	Marshmallow root, nat...	270467	1
Bombastus	Marshmallow root, nat...	276741	1
Caelo	Marshmallow root, nat...	270114	1
Bombastus	Marshmallow root, pee...	273458	1
Caelo	Marshmallow root, pee...	26091201	1
Caelo	Marshmallow root, pee...	11101907	7
Caelo	Marshmallow root, pee...	11101804	1
Caelo	Marshmallow root, pee...	6071A130116	10
Caelo	Marshmallow root, pee...	12147311	1
Caelo	Marshmallow root, pee...	12147311	7
Caelo	Marshmallow root, pee...	13057103	1
Caelo	Marshmallow root, pee...	12368906	1
Caelo	Marshmallow root, pee...	15104503	1
Caelo	Marshmallow root, pee...	11101905	1
Caelo	Marshmallow root, pee...	11101804	1
Gehe	Marshmallow root, pee...	6071A120306	2
Klenk	Marshmallow root, pee...	6071A130612	4
Klenk	Marshmallow root, pee...	6074B100416	1
Klenk	Marshmallow root, pee...	6071A120314	10
Klenk	Marshmallow root, pee...	6071A-130408	1
Klenk	Marshmallow root, pee...	A130408	3
Klenk	Marshmallow root, pee...	6071A-120314	1
Klenk	Marshmallow root, pee...	130116	1
Klenk	Marshmallow root, pee...	6071a130408	1
Klenk	Marshmallow root, pee...	6071B091207	1
Phönix	Marshmallow root, pee...	6071a120314	1
Phönix	Marshmallow root, pee...	2090413	1
Phönix	Marshmallow root, pee...	6071A130408	14
Caelo	Masterwort root, cut	12101806	2
Caelo	Masterwort root, cut	12101808	1
Caelo	Masterwort root, cut	13132002	1
Caelo	Masterwort root, cut	13341201	1
Caelo	Masterwort root, cut	1210801	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Masterwort root, cut	12101807	2
Galke	Masterwort root, cut	18411	1
Galke	Masterwort root, cut	23074	1
Caelo	Maté leaf, cut	12133803	3
Caelo	Maté leaf, cut	2141A120821	2
Caelo	Maté leaf, cut	13061202	1
Caelo	Maté leaf, cut	12133806	1
Caelo	Maté leaf, cut	13118003	4
Caelo	Maté leaf, cut	12133801	3
Caelo	Maté leaf, cut	11091710	1
Caelo	Maté leaf, cut	12133804	7
Caelo	Maté leaf, cut	13118001	1
Caelo	Maté leaf, cut	12133807	7
Caesar & Loretz GmbH,...	Maté leaf, cut	13118002	10
Galke	Maté leaf, cut	22365	1
Klenk	Maté leaf, cut	2141A111213	16
Klenk	Maté leaf, cut	2131A111213	1
Klenk	Maté leaf, cut	2141A-111213	1
Klenk	Maté leaf, cut	2141a111213	1
Klenk	Matricaria flower	1290A-120620	1
Bahnhof-Apotheke	Matricaria flower	11-121024	1
Bombastus	Matricaria flower	268712	1
Bombastus	Matricaria flower	274106	1
Bombastus	Matricaria flower	273667	1
Bombastus	Matricaria flower	276095	5
Bombastus	Matricaria flower	276307	1
Bombastus	Matricaria flower	271781	1
Bombastus	Matricaria flower	281103	2
Bombastus	Matricaria flower	287855	1
Bombastus	Matricaria flower	299185	1
Bombastus	Matricaria flower	283710	2
Bombastus	Matricaria flower	274105	1
Bombastus	Matricaria flower	273388	1
Bombastus	Matricaria flower	277997	1
Bombastus	Matricaria flower	265419	1
Bombastus	Matricaria flower	268408	1
Bombastus	Matricaria flower	268408	1
Bombastus	Matricaria flower	277959	2
Bombastus	Matricaria flower	264997	1
Caelo	Matricaria flower	12294802	15
Caelo	Matricaria flower	12294804	1
Caelo	Matricaria flower	11169607	1
Caelo	Matricaria flower	13061201	1
Caelo	Matricaria flower	10081201	1
Caelo	Matricaria flower	22081202	1
Caelo	Matricaria flower	12059606	2
Caelo	Matricaria flower	5081201	1
Caelo	Matricaria flower	12244802	4
Caelo	Matricaria flower	27091203	1
Caelo	Matricaria flower	11214810	1
Caelo	Matricaria flower	11101203	1
Caelo	Matricaria flower	17101204	1
Caelo	Matricaria flower	12244803	3
Caelo	Matricaria flower	12111903	2
Caelo	Matricaria flower	13111201	1
Caelo	Matricaria flower	16111202	1
Caelo	Matricaria flower	19111207	1
Caelo	Matricaria flower	22111201	1
Caelo	Matricaria flower	22111202	1
Caelo	Matricaria flower	12299701	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Matricaria flower	22011303	1
Caelo	Matricaria flower	12299703	2
Caelo	Matricaria flower	20021313	1
Caelo	Matricaria flower	13031306	1
Caelo	Matricaria flower	19041306	1
Caelo	Matricaria flower	12361701	3
Caelo	Matricaria flower	13014501	1
Caelo	Matricaria flower	12337601	1
Caelo	Matricaria flower	IntCh:313011	1
Caelo	Matricaria flower	26081303	1
Caelo	Matricaria flower	12337610	1
Caelo	Matricaria flower	12361704	1
Caelo	Matricaria flower	12337608	1
Caelo	Matricaria flower	12361707	2
Caelo	Matricaria flower	13210901	3
Caelo	Matricaria flower	12361706	1
Caelo	Matricaria flower	13011406	1
Caelo	Matricaria flower	13288405	3
Caelo	Matricaria flower	14276804	3
Caelo	Matricaria flower	15090003	2
Caelo	Matricaria flower	15258504	1
Caelo	Matricaria flower	15258505	1
Caelo	Matricaria flower	11218501	1
Caelo	Matricaria flower	13210906	1
Caelo	Matricaria flower	12361702	6
Caelo	Matricaria flower	12361707	4
Caelo	Matricaria flower	13210905	3
Caelo	Matricaria flower	12244803	1
Caelo	Matricaria flower	13210901-3478312171	1
Caelo	Matricaria flower	12337607	2
Caelo	Matricaria flower	12244805	4
Caelo	Matricaria flower	12244804	2
Caelo	Matricaria flower	12361706	3
Caelo	Matricaria flower	13210905	1
Caelo	Matricaria flower	13210903	1
Caelo	Matricaria flower	13210901-3546411013	1
Caelo	Matricaria flower	AKD5	1
Defektur	Matricaria flower	56/12	1
Defektur	Matricaria flower	10/13	1
Defektur	Matricaria flower	29/13	1
Defektur	Matricaria flower	59/13	1
Fagron	Matricaria flower		1
Finze	Matricaria flower	1290B101122	1
Finze	Matricaria flower	12361703	6
Galke	Matricaria flower	18471	5
Galke	Matricaria flower	18803	1
Galke	Matricaria flower	21652	1
Gehe	Matricaria flower	11214802	1
Gehe	Matricaria flower	11255204	1
Gehe	Matricaria flower	12133009	1
Gehe	Matricaria flower	12337605	1
Hepart AG	Matricaria flower	B-477 ,kBA	1
Klenk	Matricaria flower	1290B140123	2
k	Matricaria flower	1290A140513	1
Klenk	Matricaria flower	1290A150618	1
Klenk	Matricaria flower	1290A20404	1
Klenk	Matricaria flower	1290A120404	1
Klenk	Matricaria flower	1290A120404	6
Klenk	Matricaria flower	2310211452	1
Klenk	Matricaria flower	27111204	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Matricaria flower	1290A120403	3
Klenk	Matricaria flower	1290A12061	1
Klenk	Matricaria flower	1290A110825	1
Klenk	Matricaria flower	1290B130415	39
Klenk	Matricaria flower	1290A120601	2
Klenk	Matricaria flower	B130415	2
Klenk	Matricaria flower	11101302	1
Klenk	Matricaria flower	14111314	1
Klenk	Matricaria flower	A130502	1
Klenk	Matricaria flower	A130516	1
Klenk	Matricaria flower	A120529	1
Klenk	Matricaria flower	16121301	1
Klenk	Matricaria flower	1290A130516	3
Klenk	Matricaria flower	1290A130502	1
Klenk	Matricaria flower	1290A130516	9
Klenk	Matricaria flower	A120529	1
Klenk	Matricaria flower	1290A130502	1
Klenk	Matricaria flower	1290B140624	1
Klenk	Matricaria flower	1290A140508	1
Klenk	Matricaria flower	1290A120620	13
Klenk	Matricaria flower	1290A120529	1
Klenk	Matricaria flower	4100113002	2
Klenk	Matricaria flower	1290A120601	14
Klenk	Matricaria flower	1290A110421	1
Klenk	Matricaria flower	1290B130415	3
Klenk	Matricaria flower	1290a120620	1
Klenk	Matricaria flower	1290A110607	1
Klenk	Matricaria flower	1290A120529	5
Phönix	Matricaria flower	1300A120426	1
Sanacorp	Matricaria flower	12294804	6
Sanacorp	Matricaria flower	12294809	3
Sanacorp	Matricaria flower	1300A120725	2
Sanacorp	Matricaria flower	1290B140123	2
Spangropharm	Matricaria flower	11169606	1
Wolf	Matricaria flower	23242	1
Caelo	Meadowsweet flower, r...	9326211	2
Caelo	Meadowsweet flower, r...	9326213	2
Caelo	Meadowsweet flower, r...	10349305	1
Caelo	Meadowsweet flower, r...	1227501	1
Caelo	Meadowsweet flower, r...	12275701	2
Caelo	Meadowsweet flower, r...	10051301	1
Caelo	Meadowsweet flower, r...	10349308	1
Caelo	Meadowsweet flower, r...	1225702	1
Caelo	Meadowsweet flower, r...	12275703	3
Caelo	Meadowsweet flower, r...	12275704	4
Caelo	Meadowsweet flower, r...	12275702	1
Caelo	Meadowsweet flower, r...	10349302	2
Caelo	Meadowsweet flower, r...	10349307	2
Caelo	Meadowsweet flower, r...	12275704-3372319032	1
Klenk	Meadowsweet flower, r...	A120312	1
Kräuter Schulte	Meadowsweet flower, r...	51369	1
Kräuter Schulte	Meadowsweet flower, r...	53473	1
-	Meadowsweet herb, cut	1511M-01685	1
-	Meadowsweet herb, cut	130849	1
Anzag	Meadowsweet herb, cut	10381604	5
Caelo	Meadowsweet herb, cut	10381602	3
Caelo	Meadowsweet herb, cut	10381601	1
Caelo	Meadowsweet herb, cut	12188704	2
Caelo	Meadowsweet herb, cut	12188703	1
Caelo	Meadowsweet herb, cut	12188803	10

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Meadowsweet herb, cut	4912E-01685	1
Caelo	Meadowsweet herb, cut	12188801	1
Caelo	Meadowsweet herb, cut	12188807	1
Caelo	Meadowsweet herb, cut	12188702	1
Caelo	Meadowsweet herb, cut	12188805	13
Caelo	Meadowsweet herb, cut	12188806	3
Caelo	Meadowsweet herb, cut	62487517	1
Galke	Meadowsweet herb, cut	20358	1
Sanacorp	Meadowsweet herb, cut	4541A120313	2
Weltecke	Meadowsweet herb, cut	67010413	1
-	Melilot herb, cut	811Q-01664	1
Anzag ek:3,13EUR 15.09.12	Melilot herb, cut	11307605	4
Caelo	Melilot herb, cut	8061204	1
Caelo	Melilot herb, cut	19071201	1
Caelo	Melilot herb, cut	24081202	1
Caelo	Melilot herb, cut	11307606	6
Caelo	Melilot herb, cut	11307601	1
Caelo	Melilot herb, cut	12231703	3
Caelo	Melilot herb, cut	12289202	8
Caelo	Melilot herb, cut	11307607	1
Caelo	Melilot herb, cut	122891202	1
Caelo	Melilot herb, cut	12289203	5
Caelo	Melilot herb, cut	25091301	1
Caelo	Melilot herb, cut	22111303	1
Caelo	Melilot herb, cut	12289206	1
Caelo	Melilot herb, cut	12289207	1
Caelo	Melilot herb, cut	12289201	1
Caelo	Melilot herb, cut	12231701	3
Caelo	Melilot herb, cut	107063	1
Caelo	Melilot herb, cut	12289205	4
Gehe	Melilot herb, cut	110324	1
Klenk	Melilot herb, cut	4151A110324	8
Klenk	Melilot herb, cut	4151A120912	1
Klenk	Melilot herb, cut	A110324	6
Phönix	Melilot herb, cut	1237903	1
-	Melissa leaf, cut	131146	1
Alfred Galke	Melissa leaf, cut	D-NI-1-9516-BC	1
Bahnhof-Apotheke	Melissa leaf, cut	17-120917	1
Bombastus	Melissa leaf, cut	270044	1
Bombastus	Melissa leaf, cut	271499	2
Bombastus	Melissa leaf, cut	277722	1
Caelo	Melissa leaf, cut		1
Caelo	Melissa leaf, cut	1009	1
Caelo	Melissa leaf, cut	CH.111111	1
Caelo	Melissa leaf, cut	12032303	1
Caelo	Melissa leaf, cut	12032309	1
Caelo	Melissa leaf, cut	12032307	2
Caelo	Melissa leaf, cut	12032316	3
Caelo	Melissa leaf, cut	25021301	1
Caelo	Melissa leaf, cut	12032319	5
Caelo	Melissa leaf, cut	19041303	1
Caelo	Melissa leaf, cut	25061303	1
Caelo	Melissa leaf, cut	13030805	1
Caelo	Melissa leaf, cut	14111319	1
Caelo	Melissa leaf, cut	24011407	1
Caelo	Melissa leaf, cut	13214705	1
Caelo	Melissa leaf, cut	13214720	1
Caelo	Melissa leaf, cut	10310919	1
Caelo	Melissa leaf, cut	12032318	1
Caelo	Melissa leaf, cut	13030803	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Melissa leaf, cut	2161a121009	1
galke	Melissa leaf, cut	20867	1
Gehe	Melissa leaf, cut	12032314	4
Klenk	Melissa leaf, cut	2161A121206	2
Klenk	Melissa leaf, cut	2161A151209	1
Klenk	Melissa leaf, cut	111207	1
Klenk	Melissa leaf, cut	2807211503	1
Klenk	Melissa leaf, cut	2161A111207	15
Klenk	Melissa leaf, cut	2161A110818	1
Klenk	Melissa leaf, cut	27091201	1
Klenk	Melissa leaf, cut	2161A120718	11
Klenk	Melissa leaf, cut	2161A121009	14
Klenk	Melissa leaf, cut	2161A121009/PN:1198	1
Klenk	Melissa leaf, cut	2161A121029	4
Klenk	Melissa leaf, cut	2161A101216	1
Caelo	Melissa leaf, cut	13214707	1
Caelo	Melissa leaf, cut	12032310	1
Fagron	Methadone hydrochloride	18C01-B05-346737	1
Fagron	Methadone hydrochloride	18G02-B02-355989	4
Bombastus	Methadone hydrochloride	14C24-B01-292858	6
Caelo	Methadone hydrochloride	15244702	1
Caelo	Methadone hydrochloride	16135312	3
Caelo	Methadone hydrochloride	16135311	4
Caelo	Methadone hydrochloride	1081801	1
Caelo	Methadone hydrochloride	10076407	1
Caelo	Methadone hydrochloride	11227507	1
Caelo	Methadone hydrochloride	12171907	1
Caelo	Methadone hydrochloride	12171902	1
Caelo	Methadone hydrochloride	12171914	1
Caelo	Methadone hydrochloride	17011406	1
Caelo	Methadone hydrochloride	12344818	1
Caelo	Methadone hydrochloride	12344819	1
Caelo	Methadone hydrochloride	13266502	2
Caelo	Methadone hydrochloride	13266511	2
Caelo	Methadone hydrochloride	15244705	2
Caelo	Methadone hydrochloride	15244710	4
Caelo	Methadone hydrochloride	15244701	1
Caelo	Methadone hydrochloride	15244717	6
Caelo	Methadone hydrochloride	15244715	3
Caelo	Methadone hydrochloride	15244718	1
Caelo	Methadone hydrochloride	16135308	3
Caelo	Methadone hydrochloride	16135307	2
Caelo	Methadone hydrochloride	16135303	1
Caelo	Methadone hydrochloride	16135305	6
Caelo	Methadone hydrochloride	16135301	1
Caelo	Methadone hydrochloride	28041725	1
Caelo	Methadone hydrochloride	16135310	4
Caelo	Methadone hydrochloride	28061702	1
Caelo	Methadone hydrochloride	16135315	1
Caelo	Methadone hydrochloride	16135317	2
Caelo	Methadone hydrochloride	16135324	3
Caelo	Methadone hydrochloride	16135329	9
Caelo	Methadone hydrochloride	1613529	1
Caelo	Methadone hydrochloride	7091708	1
Caelo	Methadone hydrochloride	25111701	1
Caelo	Methadone hydrochloride	17239502	3
Caelo	Methadone hydrochloride	1729504	1
Caelo	Methadone hydrochloride	2912161	1
Caelo	Methadone hydrochloride	17239506	7
Caelo	Methadone hydrochloride	16135323	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Methadone hydrochloride	17239507	4
Caelo	Methadone hydrochloride	23021802	1
Caelo	Methadone hydrochloride	17239510	5
Caelo	Methadone hydrochloride	17239501	1
Caelo	Methadone hydrochloride	17051801	1
Caelo	Methadone hydrochloride	1723	1
Caelo	Methadone hydrochloride	17239518	3
Caelo	Methadone hydrochloride	17239514	1
Caelo	Methadone hydrochloride	1723509	1
Caelo	Methadone hydrochloride	3111806	1
Caelo	Methadone hydrochloride	18186608	5
Caelo	Methadone hydrochloride	19011913	1
Caelo	Methadone hydrochloride	31011901	1
Caelo	Methadone hydrochloride	18132406	3
Caelo	Methadone hydrochloride	18132413	6
Caelo	Methadone hydrochloride	18186607	1
Caelo	Methadone hydrochloride	18c01b05350572	1
Caelo	Methadone hydrochloride	18g02-b02-355992	1
Caelo	Methadone hydrochloride	18g02-b02355992	1
Caelo	Methadone hydrochloride	18132407	1
Caelo	Methadone hydrochloride	18132416	1
Caelo	Methadone hydrochloride	19149406	1
Caelo	Methadone hydrochloride	15244720	1
Caelo	Methadone hydrochloride	20170728/Ma2	1
Caelo	Methadone hydrochloride	15244713	4
Caelo	Methadone hydrochloride	18186601	7
Caelo	Methadone hydrochloride	57(18132413)	1
Caelo	Methadone hydrochloride	14C24-B01-292860	1
Caelo	Methadone hydrochloride	1327H051	1
Caelo	Methadone hydrochloride	13266521	1
Caelo	Methadone hydrochloride	18132405	4
Caelo	Methadone hydrochloride	19149402	2
Caelo	Methadone hydrochloride	13266515	1
Caelo	Methadone hydrochloride	16135327	11
Caelo	Methadone hydrochloride	17I15-B02-339523	4
Caelo	Methadone hydrochloride	17239512	9
Caelo	Methadone hydrochloride	58(18132417)	1
Caelo	Methadone hydrochloride	16135302	1
Caelo	Methadone hydrochloride	16135318	5
Caelo	Methadone hydrochloride	16135326	8
Caelo	Methadone hydrochloride	16135325,170814MHC	1
Caelo	Methadone hydrochloride	16135332	8
Caelo	Methadone hydrochloride	172329504	1
Caelo	Methadone hydrochloride	16135328	1
Caelo	Methadone hydrochloride	180219MC/17239506	1
Caelo	Methadone hydrochloride	17239503	3
Caelo	Methadone hydrochloride	18186604	1
Caelo	Methadone hydrochloride	12344802	1
Caelo	Methadone hydrochloride	15244709	2
Caelo	Methadone hydrochloride	16135330	5
Caelo	Methadone hydrochloride	171920-0004	1
Caelo	Methadone hydrochloride	18132412	5
Caelo	Methadone hydrochloride	13266514	1
Caelo	Methadone hydrochloride	15I24-B07-317266	1
Caelo	Methadone hydrochloride	16F24-B02-323184	1
Caelo	Methadone hydrochloride	18132409	1
Caelo	Methadone hydrochloride	12171906	2
Caelo	Methadone hydrochloride	12344816	3
Caelo	Methadone hydrochloride	13266501	1
Caelo	Methadone hydrochloride	13266505	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Methadone hydrochloride	13266518	3
Caelo	Methadone hydrochloride	15215501	1
Caelo	Methadone hydrochloride	15244704	4
Caelo	Methadone hydrochloride	15244706	3
Caelo	Methadone hydrochloride	16208016	1
Caelo	Methadone hydrochloride	17239508	1
Caelo	Methadone hydrochloride	18132408	5
Caesar & Loretz GmbH	Methadone hydrochloride	18132417	3
Dr. Wolff	Methadone hydrochloride	16F24-B02	1
Ebert-Jacobi	Methadone hydrochloride	16135306	1
Euro OTC	Methadone hydrochloride	14C24-B01	2
Fagron	Methadone hydrochloride	1437H011	1
Fagro/ Noweda	Methadone hydrochloride	17/15-B02-339527	1
Fagro//Noweda	Methadone hydrochloride	15/24-B07-317267	1
Fagro/Jenne	Methadone hydrochloride	17I15-B02-339525	2
Fagron	Methadone hydrochloride	12B21N03	1
Fagron	Methadone hydrochloride	11G11-N02	1
Fagron	Methadone hydrochloride	17I15-B02-339521	1
Fagron	Methadone hydrochloride	12H07-N07	1
Fagron	Methadone hydrochloride	20130912-6	1
Fagron	Methadone hydrochloride	12H07-N05	4
Fagron	Methadone hydrochloride	1213E-02949	1
Fagron	Methadone hydrochloride	9041306	1
Fagron	Methadone hydrochloride	171920-0009	1
Fagron	Methadone hydrochloride	1225H008	1
Fagron	Methadone hydrochloride	13B06-N02	5
Fagron	Methadone hydrochloride	13F17-N02	6
Fagron	Methadone hydrochloride	25091307	1
Fagron	Methadone hydrochloride	414022-1-P	1
Fagron	Methadone hydrochloride	11D07-N09	1
Fagron	Methadone hydrochloride	13I24-B06-286908	1
Fagron	Methadone hydrochloride	25091406	1
Fagron	Methadone hydrochloride	13J24-B06-286907	1
Fagron	Methadone hydrochloride	1327h051	1
Fagron	Methadone hydrochloride	14C24-B01-292857	4
Fagron	Methadone hydrochloride	4031517	1
Fagron	Methadone hydrochloride	14H15-B01-299381	1
Fagron	Methadone hydrochloride	29051502	1
Fagron	Methadone hydrochloride	15B24-B02-304724	6
Fagron	Methadone hydrochloride	8081501	1
Fagron	Methadone hydrochloride	1437H012	2
Fagron	Methadone hydrochloride	15E29-B02-313031	1
Fagron	Methadone hydrochloride	13J24B06286910	1
Fagron	Methadone hydrochloride	1514H042	3
Fagron	Methadone hydrochloride	2877	1
Fagron	Methadone hydrochloride	1608H002	2
Fagron	Methadone hydrochloride	16F24-B02-323185	1
Fagron	Methadone hydrochloride	16K01-B04-329933	2
Fagron	Methadone hydrochloride	16K01B04	1
Fagron	Methadone hydrochloride	16K01-B04-329934	2
Fagron	Methadone hydrochloride	16K01-B04	2
Fagron	Methadone hydrochloride	17C24-B05-334309	5
Fagron	Methadone hydrochloride	16-k01-B04-329937	1
Fagron	Methadone hydrochloride	17I15-B02-339529	2
Fagron	Methadone hydrochloride	17c24b05334309	1
Fagron	Methadone hydrochloride	17I15-B02-339521	3
Fagron	Methadone hydrochloride	17/15-B02-339521	2
Fagron	Methadone hydrochloride	17I15-B02-343153	1
Fagron	Methadone hydrochloride	17I15-B02-343153	1
Fagron	Methadone hydrochloride	17I15-B02-343154	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Methadone hydrochloride	339527	1
Fagron	Methadone hydrochloride	17/15-B02-343153	1
Fagron	Methadone hydrochloride	18C01-B05-350573	1
Fagron	Methadone hydrochloride	18G02-B02	2
Fagron	Methadone hydrochloride	1801h11	1
Fagron	Methadone hydrochloride	1801h011	1
Fagron	Methadone hydrochloride	18G02-B02-355993	2
Fagron	Methadone hydrochloride	18G02-B02-355994	1
Fagron	Methadone hydrochloride	18c01-b05-350572	1
Fagron	Methadone hydrochloride	18gb02-35599202-	1
Fagron	Methadone hydrochloride	16K01-B04-329936	1
Fagron	Methadone hydrochloride	19D09-B03-364518	1
Fagron	Methadone hydrochloride	19D09-B03-364519	1
Fagron	Methadone hydrochloride	13J24-B06-286908	1
Fagron	Methadone hydrochloride	1409H043	1
Fagron	Methadone hydrochloride	15E29-B02-313098	3
Fagron	Methadone hydrochloride	15B24-B02-313097	1
Fagron	Methadone hydrochloride	15E29_B02_309070	1
Fagron	Methadone hydrochloride	1316H037	4
Fagron	Methadone hydrochloride	17115-B02	1
Fagron	Methadone hydrochloride	15I24-B07	1
Fagron	Methadone hydrochloride	16F24-B02-323186	1
Fagron	Methadone hydrochloride	17C24-B05-334311	2
Fagron	Methadone hydrochloride	18G02-B02-351285	1
Fagron	Methadone hydrochloride	16f24-b02-323184	1
Fagron	Methadone hydrochloride	17C24-B05-335711	7
Fagron	Methadone hydrochloride	17I15W02	1
Fagron	Methadone hydrochloride	350571	1
Fagron	Methadone hydrochloride	16k01-b04-329933	1
Fagron	Methadone hydrochloride	12A05-No2	1
Fagron	Methadone hydrochloride	14H15-B01-299382	6
Fagron	Methadone hydrochloride	15E29-B02-309070	2
Fagron	Methadone hydrochloride	18C01-B05-350571	6
Fagron	Methadone hydrochloride	16F24-B02-323182	1
Fagron	Methadone hydrochloride	170427MH/1608H002	1
Fagron	Methadone hydrochloride	16F24-B02-329935	1
Fagron	Methadone hydrochloride	17I15-B02	2
Fagron	Methadone hydrochloride	18G02-B02-355991	1
Fagron	Methadone hydrochloride	14H15-B01	1
Fagron	Methadone hydrochloride	16F24-B02-326207	2
Fagron	Methadone hydrochloride	1718H028	6
Fagron	Methadone hydrochloride	12b21-n03	1
Fagron	Methadone hydrochloride	16B16-B02-318420	2
Fagron	Methadone hydrochloride	1715-B02-339525	2
Fagron	Methadone hydrochloride	15-B02-339525	1
Fagron	Methadone hydrochloride	1715-B02-343150	1
Fagron	Methadone hydrochloride	15-B02-343150	1
Fagron	Methadone hydrochloride	18G02-B02-355990	5
Fagron	Methadone hydrochloride	17I15-B02-343150	1
Fagron	Methadone hydrochloride	19D09-B03-364513	2
Fagron	Methadone hydrochloride	16K01-B04-329937	2
Gatt-Koller	Methadone hydrochloride	1801702	1
gehe	Methadone hydrochloride	16135316	3
Gehe	Methadone hydrochloride	18132403	6
Gehe/Noweda	Methadone hydrochloride	16135319	2
Hedinger/ Sanacorp	Methadone hydrochloride	15215505	3
Jenne	Methadone hydrochloride	15B24-B02	1
Klosterring	Methadone hydrochloride	17I15-B02-343151	4
L30	Methadone hydrochloride	67055	22
Fagron	Methadone hydrochloride	17c24-b05	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Methadone hydrochloride	12171918	1
Caelo	Methadone hydrochloride	12344812	2
Caelo	Methadone hydrochloride	12344807	1
Caelo	Methadone hydrochloride	12344814	2
Caelo	Methadone hydrochloride	13266504	2
Caelo	Methadone hydrochloride	16135325	1
Caelo	Methadone hydrochloride	17C24-B05	2
Euro OTC	Methadone hydrochloride	16135304	5
Phoenix	Methadone hydrochloride	16125317	1
Phönix	Methadone hydrochloride	16135309	2
Caelo	Methadone hydrochloride	17239504	5
Fagron	Methadone hydrochloride	16F24B02323184	2
Sanacorp	Methadone hydrochloride	12171913	1
Sanacorp	Methadone hydrochloride	12344806	2
Siegfried Ltd	Methadone hydrochloride	12B21-N03	1
Siegfried Ltd, Divisi...	Methadone hydrochloride	15244712	1
Th. Geyer	Methadone hydrochloride	70617	1
Th. Geyer	Methadone hydrochloride		1
Th. Geyer	Methadone hydrochloride	67047	2
Th. Geyer	Methadone hydrochloride	56(070245)	1
Th. Geyer	Methadone hydrochloride	70245	68
Th. Geyer	Methadone hydrochloride	70246	1
VDL;87,00EUR;08.09.14	Methadone hydrochloride	12344821	1
Caelo	Methylrosanilinium ch...	9238107	1
Caelo	Methylrosanilinium ch...	12H28-N06	1
Caelo	Methylrosanilinium ch...	3455360	1
Caelo	Methylrosanilinium ch...	13184801	1
Caelo	Methylrosanilinium ch...	12H28-No6	1
Caelo	Methylrosanilinium ch...	9238109	1
Caelo	Methylrosanilinium ch...	9238106	1
Fagron	Methylrosanilinium ch...	12H28_N06	1
Fagron	Methylrosanilinium ch...	13H28-N03	2
Fagron	Methylrosanilinium ch...	1989	2
Fagron	Methylrosanilinium ch...	13G03N11	1
Fagron	Methylrosanilinium ch...	13H28-No3	1
Fagron	Methylrosanilinium ch...	13G03-N011	1
Fagron	Methylrosanilinium ch...	13H28-N03	18
Fagron	Methylrosanilinium ch...	13H28-N03-0161-1030	1
Fagron	Methylrosanilinium ch...	12-17-N050109-140	1
Fagron	Methylrosanilinium ch...	12D19-N01	1
Fagron	Methylrosanilinium ch...	13H28-N03	1
Fagron	Methylrosanilinium ch...	13G03-N11	1
Fagron	Methylrosanilinium ch...	12I17-N05	1
Noweda	Methylrosanilinium ch...	9238104	1
Noweda	Methylrosanilinium ch...	12H28-N06	1
Noweda	Methylrosanilinium ch...	2159	2
Caelo	Methylrosanilinium ch...	12/17-N05	1
phönix	Methylrosanilinium ch...	13184811	1
Fagron	Midazolam	14C12-B31-313222	1
Fagron	Midazolam	16J03-B09-326963	1
Caelo	Midazolam hydrochloride	2061508	1
Caelo	Midazolam hydrochloride	15224603	1
Caelo	Midazolam hydrochloride	15224607	2
Caelo	Midazolam hydrochloride	15224614	2
Caelo	Midazolam hydrochloride	14339002	1
Caelo	Midazolam hydrochloride	15224616	3
Caelo	Midazolam hydrochloride	16290605	8
Caelo	Midazolam hydrochloride	17168009	1
Caelo	Midazolam hydrochloride	11184705	1
Caelo	Midazolam hydrochloride	17168007	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Midazolam hydrochloride	15224605	1
Caelo	Midazolam hydrochloride	14339009	1
Caelo	Midazolam hydrochloride	83600116001	1
Caelo	Midazolam hydrochloride	14339015	2
Caelo/ Noweda	Midazolam hydrochloride	17168006	3
Eurho/Phoenix	Midazolam hydrochloride	12L17-N10	1
Fagron	Midazolam hydrochloride	9D27-N01	2
Fagron	Midazolam hydrochloride	11A31-N01	1
Fagron	Midazolam hydrochloride	15H04-B03-314396	7
Fagron	Midazolam hydrochloride	400101	1
Fagron	Midazolam hydrochloride	18B28-B05-354856	1
Fagron	Midazolam hydrochloride	18F19-B02	1
Fagron	Midazolam hydrochloride	14H05-B08-297982	1
Fagron	Midazolam hydrochloride	17K21-B05-347538	1
Fagron	Midazolam hydrochloride	18F19B02-354857	1
Fagron	Midazolam hydrochloride	16C14-B12-332469	1
JENNE	Midazolam hydrochloride	17168003	5
Noweda	Midazolam hydrochloride	17168011	1
PHÖNIX	Midazolam hydrochloride	18B28-B05	1
Anzag ek:2,64EUR 16.07.12	Mistletoe, cut	10273417	1
Aurica/Phönix	Mistletoe, cut	6110801	1
Bombastus	Mistletoe, cut	277432	2
Caelo	Mistletoe, cut	29061201	1
Caelo	Mistletoe, cut	10273412	1
Caelo	Mistletoe, cut	10081205	1
Caelo	Mistletoe, cut	10091201	1
Caelo	Mistletoe, cut	11294003	2
Caelo	Mistletoe, cut	23111204	1
Caelo	Mistletoe, cut	10273418	1
Caelo	Mistletoe, cut	10273420	5
Caelo	Mistletoe, cut	12011301	1
Caelo	Mistletoe, cut	11266704	14
Caelo	Mistletoe, cut	11021303	1
Caelo	Mistletoe, cut	11266708	8
Caelo	Mistletoe, cut	11266705	3
Caelo	Mistletoe, cut	18031303	1
Caelo	Mistletoe, cut	11266710	7
Caelo	Mistletoe, cut	6061306	1
Caelo	Mistletoe, cut	17061304	1
Caelo	Mistletoe, cut	26071302	1
Caelo	Mistletoe, cut	29071302	1
Caelo	Mistletoe, cut	29081302	1
Caelo	Mistletoe, cut	28101304	1
Caelo	Mistletoe, cut	29101302	1
Caelo	Mistletoe, cut	20121303	1
Caelo	Mistletoe, cut	27121305	1
Caelo	Mistletoe, cut	24011401	1
Caelo	Mistletoe, cut	14292506	2
Caelo	Mistletoe, cut	14292514	1
Caelo	Mistletoe, cut	11266714	4
Caelo	Mistletoe, cut	11266703	3
Caelo	Mistletoe, cut	11266712-3450311162	1
Caelo	Mistletoe, cut	11266702	4
Caelo	Mistletoe, cut	10273407	1
Caelo	Mistletoe, cut	11294004	5
Caelo	Mistletoe, cut	3813E-01695	1
Caelo	Mistletoe, cut	4313E-01695	1
Caelo	Mistletoe, cut	11266713	2
Galke	Mistletoe, cut	20328	1
Galke	Mistletoe, cut	22012	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Gesundform	Mistletoe, cut	216482	1
Haustee	Mistletoe, cut	57010507	1
Caelo	Mistletoe, cut	11294005	15
Klenk	Mistletoe, cut	4691A120507	2
Klenk	Mistletoe, cut	4691A110816	2
Klenk	Mistletoe, cut	1512211695	1
Klenk	Mistletoe, cut	2901311695	1
Klenk	Mistletoe, cut	110816	1
Klenk	Mistletoe, cut	4691A130307	7
Klenk	Mistletoe, cut	4691A121122	11
Klenk	Mistletoe, cut	4961A120419	1
Klenk	Mistletoe, cut	4691a130307	1
Klenk	Mistletoe, cut	4691A-120507	1
Klenk	Mistletoe, cut	4691a121122	1
Klenk	Mistletoe, cut	4691A121122-35454110	1
Noweda	Mistletoe, cut	11294001	1
Caelo	Mistletoe, cut	11266709	10
Caelo	Mistletoe, cut	11266712	8
Klenk	Mistletoe, cut	4691A120419	6
Spangropharm	Mistletoe, cut	10273408	1
Caelo	Molecular distilled g...	11160012	1
Noweda	Molecular distilled g...	11160010	1
Caelo	Morphine hydrochloride	12318101	1
Caelo	Morphine hydrochloride	13081310	1
Caelo	Morphine hydrochloride	12104409	1
Caelo	Morphine hydrochloride	14238604	1
Caelo	Morphine hydrochloride	15199705	1
Caelo	Morphine hydrochloride	15199705Nr. 2	1
Caelo	Morphine hydrochloride	15199705Nr. 3	1
Caelo	Morphine hydrochloride	15199711	4
Caelo	Morphine hydrochloride	15199709	1
Caelo	Morphine hydrochloride	1543904	1
Caelo	Morphine hydrochloride	14238619	1
Caelo	Morphine hydrochloride	15439409	1
Caelo	Morphine hydrochloride	15439406	3
Caelo	Morphine hydrochloride	13125208	1
Caelo	Morphine hydrochloride	15439405	2
Caelo	Morphine hydrochloride	15439402	1
Caelo	Morphine hydrochloride	16184602	2
Caelo	Morphine hydrochloride	16184605	2
Caelo	Morphine hydrochloride	14081701	1
Caelo	Morphine hydrochloride	16184610	2
Caelo	Morphine hydrochloride	16184609	2
Caelo	Morphine hydrochloride	15199707	1
Caelo	Morphine hydrochloride	16184614	3
Caelo	Morphine hydrochloride	16184607	1
Caelo	Morphine hydrochloride	18188603	3
Caelo	Morphine hydrochloride	118188607	2
Caelo	Morphine hydrochloride	48188601	1
Caelo	Morphine hydrochloride	1818866	1
Caelo	Morphine hydrochloride	16184613	6
Caelo	Morphine hydrochloride	18188602	1
Caelo	Morphine hydrochloride	12104403	1
Caelo	Morphine hydrochloride	17258002NR: 51/18	1
Caelo	Morphine hydrochloride	18188613	1
Caelo	Morphine hydrochloride	14055084	1
Caelo	Morphine hydrochloride	18188614	2
Caelo	Morphine hydrochloride	193085002	1
Caelo	Morphine hydrochloride	13125206	1
Caelo	Morphine hydrochloride	15199713	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caesar & Loretz GmbH	Morphine hydrochloride	15199711(1)	1
Caesar & Loretz GmbH	Morphine hydrochloride	15199711(2)	1
Caesar & Loretz GmbH	Morphine hydrochloride	15199712	1
Caesar & Loretz GmbH	Morphine hydrochloride	15199711	1
Fagron	Morphine hydrochloride	11A27-N04	1
Fagron	Morphine hydrochloride	12E10N04	1
Fagron	Morphine hydrochloride	13D09-N04	1
Fagron	Morphine hydrochloride	15A12-B04-303137	1
Fagron	Morphine hydrochloride	15J27_B01_316889	1
Fagron	Morphine hydrochloride	16D21-B02-322087	1
Fagron	Morphine hydrochloride	17F22-B01-338170	2
Fagron	Morphine hydrochloride	12E10-N04	2
Fagron	Morphine hydrochloride	17C24-B03-334287	1
Fagron	Morphine hydrochloride	15I09-B08-312693	2
Fagron	Morphine hydrochloride	13H22-N12	1
Th. Geyer	Morphine hydrochloride	PH120087	1
Th. Geyer	Morphine hydrochloride	1415E-01879	1
Th. Geyer	Morphine hydrochloride	2615M-01879	1
Caelo	Morphine hydrochloride	14238617	1
Phönix	Morphine hydrochloride	17258002	3
Phönix	Morphine hydrochloride	18188601	2
Sanacorp	Morphine hydrochloride	16184612	2
Caelo	Morphine hydrochloride	15439411	1
Synop	Morphine hydrochloride	15I09-B08	1
Th. Geyer	Morphine hydrochloride	67036	5
Caelo	Morphine sulfate	17331510	2
Caelo	Motherwort herb, cut	5061203	1
Caelo	Motherwort herb, cut	12376403	1
Caelo	Motherwort herb, cut	12376408	2
Caelo	Motherwort herb, cut	12376407	1
Caelo	Motherwort herb, cut	11293004	1
Gehe	Motherwort herb, cut	12231502	3
Klenk	Motherwort herb, cut	4071A-100707	1
Phönix	Motherwort herb, cut	12231503	2
Caelo	Mullein flower, cut	12317104	1
Caelo	Mullein flower, cut	521505390	1
Caelo	Mullein flower, cut	11020802	2
Caelo	Mullein flower, cut	11020902	1
Caelo	Mullein flower, cut	16081201	1
Caelo	Mullein flower, cut	11020714	4
Caelo	Mullein flower, cut	11233401	4
Caelo	Mullein flower, cut	11366402	1
Caelo	Mullein flower, cut	12192901	3
Caelo	Mullein flower, cut	12192903	3
Caelo	Mullein flower, cut	18031301	1
Caelo	Mullein flower, cut	11233402	1
Caelo	Mullein flower, cut	11333402	1
Caelo	Mullein flower, cut	12170901	1
Caelo	Mullein flower, cut	12192904	1
Caelo	Mullein flower, cut	12192907	3
Caelo	Mullein flower, cut	13229702	1
Caelo	Mullein flower, cut	11020713	2
Caelo	Mullein flower, cut	1219203	1
Caelo	Mullein flower, cut	12192905	5
Caelo	Mullein flower, cut	11366403	1
Caelo	Mullein flower, cut	12170906	1
Caelo	Mullein flower, cut	13229701	2
Caesar/Noweda	Mullein flower, cut	2810E-01475	1
Hepart AG	Mullein flower, cut	12170904	2
Klenk	Mullein flower, cut	1650A100608	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Mullein flower, cut	1651B110203	2
Klenk	Mullein flower, cut	1650A111018	3
Klenk	Mullein flower, cut	A120612	1
Klenk	Mullein flower, cut	1650A120612	1
Klenk	Mullein flower, cut	1651B140324	2
Klenk	Mullein flower, cut	1651B150722	1
Klenk	Mullein flower, cut	1651B130820	5
Klenk	Mullein flower, cut	1651b130820	2
Klenk	Mullein flower, cut	1651B121109	22
Klenk	Mullein flower, cut	1651B120315	3
Caelo	Myrrh	11276810	1
Caelo	Myrrh	11276806	1
Caelo	Myrrh	11277111	1
Caelo	Myrrh	12269901	2
Caelo	Myrrh	12269907	1
Caelo	Myrrh	25071404	1
Caelo	Myrrh	28101401	1
Caelo	Myrrh	30121413	1
Caelo	Myrrh	12269913	1
Caelo	Myrrh	14347509	1
Caelo	Myrrh	15021410	1
Caelo	Myrrh	15312606	1
Caelo	Myrrh	12269904	4
Caelo	Myrrh	14244602	1
Caelo	Myrrh	11277111	1
Caelo	Myrrh	12244404	1
Caelo	Myrrh	12244406	1
Caelo	Myrrh	11277105	1
Caelo	Myrrh	13108701	2
Caelo	Myrrh	15021402	1
Klenk	Myrrh	3351A121004	1
Klenk	Myrrh	3351A130902	1
Klenk	Myrrh	3351A160330	3
Klenk	Myrrh	3351A120514	1
Klenk	Myrrh	3355B161010	1
phönix	Myrrh	15021411	1
phönix	Myrrh	3351a160330	1
Anzag	Nettle leaf, cut	2381-A130122	1
Anzag EK4,31 17.08.12	Nettle leaf, cut	2381A110913	19
Klenk	Nettle leaf, cut	2381a120619	4
Bahnhof-Apotheke	Nettle leaf, cut	7-121109	1
Bombastus	Nettle leaf, cut	266638	1
Bombastus	Nettle leaf, cut	270987	3
Bombastus	Nettle leaf, cut	270854	3
Bombastus	Nettle leaf, cut	273229	2
Bombastus	Nettle leaf, cut	275848	3
Bombastus	Nettle leaf, cut	280305	2
Bombastus	Nettle leaf, cut	276407	2
Bombastus	Nettle leaf, cut	266099	1
Bombastus	Nettle leaf, cut	275763	1
Caelo	Nettle leaf, cut	12183908	5
Caelo	Nettle leaf, cut	10291405	2
Caelo	Nettle leaf, cut	10282807	2
Caelo	Nettle leaf, cut	10282806	1
Caelo	Nettle leaf, cut		3
Caelo	Nettle leaf, cut	18071202	1
Caelo	Nettle leaf, cut	10291413	1
Caelo	Nettle leaf, cut	120375901	1
Caelo	Nettle leaf, cut	10291411	2
Caelo	Nettle leaf, cut	12195101	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Nettle leaf, cut	17121205	1
Caelo	Nettle leaf, cut	12184503	3
Caelo	Nettle leaf, cut	10375901	2
Caelo	Nettle leaf, cut	12184702	2
Caelo	Nettle leaf, cut	7031302	1
Caelo	Nettle leaf, cut	12184706	3
Caelo	Nettle leaf, cut	12184001	6
Caelo	Nettle leaf, cut	2051302	1
Caelo	Nettle leaf, cut	12814001	1
Caelo	Nettle leaf, cut	29071303	1
Caelo	Nettle leaf, cut	intch:313011	1
Caelo	Nettle leaf, cut	12183901	2
Caelo	Nettle leaf, cut	1283910	1
Caelo	Nettle leaf, cut	13091302	1
Caelo	Nettle leaf, cut	12183911	16
Caelo	Nettle leaf, cut	12183909	1
Caelo	Nettle leaf, cut	20111306	1
Caelo	Nettle leaf, cut	3021401	1
Caelo	Nettle leaf, cut	12034414	1
Caelo	Nettle leaf, cut	13386801	1
Caelo	Nettle leaf, cut	14344907	1
Caelo	Nettle leaf, cut	10162712	1
Caelo	Nettle leaf, cut	10291414	3
Caelo	Nettle leaf, cut	12184502	2
Caelo	Nettle leaf, cut	12184004	9
Caelo	Nettle leaf, cut	12195002	2
Caelo	Nettle leaf, cut	12183910	11
Caelo	Nettle leaf, cut	10291422	3
Caelo	Nettle leaf, cut	2381A130122	26
Caelo	Nettle leaf, cut	72085497	1
Caelo	Nettle leaf, cut	83374109	1
Caelo	Nettle leaf, cut	83142389	1
Caelo	Nettle leaf, cut	12183908-3391311070	1
Caelo	Nettle leaf, cut	12183908-3405310181	1
Caelo	Nettle leaf, cut	12183908-3443311112	1
Caelo	Nettle leaf, cut	12034403	8
Caelo	Nettle leaf, cut	12034402	3
Caesar & Loretz GmbH,...	Nettle leaf, cut	10291423	6
Galke	Nettle leaf, cut	20956	1
Galke	Nettle leaf, cut	21238	1
Galke	Nettle leaf, cut	23302	1
Gehe	Nettle leaf, cut	10162701	1
Gehe	Nettle leaf, cut	2381A120619	14
Gutenberg-Apotheke	Nettle leaf, cut	18897	1
Hepart AG	Nettle leaf, cut	P234605kbA	1
Klenk	Nettle leaf, cut	2381A-120619	1
Klenk	Nettle leaf, cut	2381A150109	1
Klenk	Nettle leaf, cut	2381A151012	1
Klenk	Nettle leaf, cut	1107211689	1
Klenk	Nettle leaf, cut	1913A-03054	1
Klenk	Nettle leaf, cut	A110913	1
Klenk	Nettle leaf, cut	2381A130703	15
Klenk	Nettle leaf, cut	A130703	1
Klenk	Nettle leaf, cut	2381a130703	1
Klenk	Nettle leaf, cut	A130122	1
Klenk	Nettle leaf, cut	2372A130703	1
Klenk	Nettle leaf, cut	2381A140221	1
Klenk	Nettle leaf, cut	2381A141124	1
Klenk	Nettle leaf, cut	2381A121010	1
Klenk	Nettle leaf, cut	114Q-03054	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Nettle leaf, cut	4513E3054	1
Klenk	Nettle leaf, cut	2381a130122	1
Klenk	Nettle leaf, cut	2381A-121010	1
Klenk	Nettle leaf, cut	2381A110809	1
Nachprüfung 8.2.13	Nettle leaf, cut	C1081	1
Noweda	Nettle leaf, cut	12195001	7
Caelo	Nettle leaf, cut	12183914	9
Sanacorp	Nettle leaf, cut	12184707	11
Sanacorp	Nettle leaf, cut	12184003	17
Caelo	Nettle leaf, cut	12184005	7
Caelo	Nettle leaf, cut	33/AD1	1
Wolf	Nettle leaf, cut	B-821	1
Wolf	Nettle leaf, cut	B821	1
Wolf	Nettle leaf, cut	P234605	10
Caelo	Nettle root, cut	10081202	1
Caelo	Nettle root, cut	11254902	3
Caelo	Nettle root, cut	11254903	5
Caelo	Nettle root, cut	11265002	5
Caelo	Nettle root, cut	11265003	2
Caelo	Nettle root, cut	6631B130610	1
Caelo	Nettle root, cut	11265006	1
Caelo	Nettle root, cut	11265004	4
Caelo	Nettle root, cut	11254904	3
Gehe	Nettle root, cut	6631B120927	5
Caelo	Nettle root, cut	6441A121024	1
Klenk	Nettle root, cut	6631N110513	1
Klenk	Nettle root, cut	6631B120416	1
Klenk	Nettle root, cut	9931B120927	1
Sanacorp	Nettle root, cut	11265001	2
Caelo	Nettle seed	12131505	1
Caelo	Nettle seed	13010607	1
Caelo	Nettle seed	20111301	1
Caelo	Nettle seed	13010612	2
Caelo	Nettle seed	17282601	1
Caelo	Nettle seed	15290602	1
Caelo	Nettle seed	16327001	2
Caelo	Nettle seed	16327003	1
Euro OTC	Nettle seed	12131507	2
Klenk	Nettle seed	7470A110418	1
Klenk	Nettle seed	2021505	1
Klenk	Nettle seed	7470A151009	1
Klenk	Nettle seed	7470A170130	1
Klenk	Nettle seed	7470A160928	2
Sanacorp	Nettle seed	13010602	1
Fagron	Nitrofurantoin	13D10-N03	1
Fagron	Nitrofurantoin	11F07-N06	3
Fagron	Nitrofurantoin	3071403	1
Fagron	Nitrofurantoin	201203080296	1
Fagron	Nitrofurantoin	15J15-B06-313939	2
Fagron	Nitrofurantoin	12F19-N02	1
Fagron	Nitrofurantoin	13A08-N01	1
Fagron	Nitrofurantoin	71/14	1
Fagron	Nitrofurantoin	15J15-B06	2
Fagron	Nitrofurantoin	13B28-N07	1
Fagron	Nitrofurantoin	2714I-03527	1
Fagron	Nitrofurantoin	15J15-B06-315225	2
Fagron	Nitrofurantoin	12C30-N03	1
Fagron	Nitrofurantoin	15J15-B06-319031	1
Fagron	Nitrofurantoin	15J15-B06-317250	2
Caelo	Nutmeg	12376805	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Nutmeg	12376802	2
Caelo	Nutmeg, powdered (spi...	12102305	2
Galke	Nutmeg, powdered (spi...	22739	1
Klenk	Nutmeg, powdered (spi...	A130304	2
Klenk	Nutmeg, powdered (spi...	7325A120903	2
Klenk	Nutmeg, powdered (spi...	7325A130304	1
Klenk	Nutmeg, powdered (spi...	7325A130515	1
Anzag 26.10.12 2.36EUR	Oak bark, cut	10348616	6
Caelo	Oak bark, cut	11351202	5
Bahnhof-Apotheke	Oak bark, cut	17-121106	1
Berkel AHK	Oak bark, cut	13360310	1
Bombastus	Oak bark, cut	272704	1
Bombastus	Oak bark, cut	265717	1
Bombastus	Oak bark, cut	274392	1
Bombastus	Oak bark, cut	274611	1
Bombastus	Oak bark, cut	279525	2
Bombastus	Oak bark, cut	229090	1
Bombastus	Oak bark, cut	286297	1
Caelo	Oak bark, cut	10348612	1
Caelo	Oak bark, cut	22081204	1
Caelo	Oak bark, cut	10348615	1
Caelo	Oak bark, cut	7021302	1
Caelo	Oak bark, cut	19032013	2
Caelo	Oak bark, cut	3041301	1
Caelo	Oak bark, cut	11351201	3
Caelo	Oak bark, cut	11351203	1
Caelo	Oak bark, cut	10238612	1
Caelo	Oak bark, cut	16081305	1
Caelo	Oak bark, cut	26081302	1
Caelo	Oak bark, cut	5091302	1
Caelo	Oak bark, cut	14111316	1
Caelo	Oak bark, cut	161212	1
Caelo	Oak bark, cut	41109-4-P	1
Caelo	Oak bark, cut	11351210	1
Caelo	Oak bark, cut	123test	1
Caelo	Oak bark, cut	13360301	1
Caelo	Oak bark, cut	1081401	1
Caelo	Oak bark, cut	280814A	1
Caelo	Oak bark, cut	13360304	1
Caelo	Oak bark, cut	13360311	1
Caelo	Oak bark, cut	13360309	1
Caelo	Oak bark, cut	10061504	1
Caelo	Oak bark, cut	14277004	1
Caelo	Oak bark, cut	14277004	2
Caelo	Oak bark, cut	15146103	1
Caelo	Oak bark, cut	15146105	4
Caelo	Oak bark, cut	15146110	1
Caelo	Oak bark, cut	15146110	1
Caelo	Oak bark, cut	15314904	1
Caelo	Oak bark, cut	15314904	3
Caelo	Oak bark, cut	15314906	1
Caelo	Oak bark, cut	15314912	3
Caelo	Oak bark, cut	18014702	1
Caelo	Oak bark, cut	19133902	1
Caelo	Oak bark, cut	18014701	1
Caelo	Oak bark, cut	15314903	1
Caelo	Oak bark, cut	15146109	2
Caelo	Oak bark, cut	10348613	2
Caelo	Oak bark, cut	11351210	8
Caelo	Oak bark, cut	11351207-3384310110	1

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Oak bark, cut	13360305	1
Caelo	Oak bark, cut	13360308	1
Caelo	Oak bark, cut	14277004	1
Caelo	Oak bark, cut	15146105	1
Caelo	Oak bark, cut	15314910	6
Caelo	Oak bark, cut	15314908	1
Caelo	Oak bark, cut	13360306	2
Caelo	Oak bark, cut	13360312	5
Caelo	Oak bark, cut	15146101	2
Caelo	Oak bark, cut	15146102	1
Caelo	Oak bark, cut	10348605	1
Caelo	Oak bark, cut	15146104	3
Caelo	Oak bark, cut	15314901	1
Caelo	Oak bark, cut	15314911	1
Caelo	Oak bark, cut	12221102	1
Caelo	Oak bark, cut	9357419	2
Caelo	Oak bark, cut	12221101	9
Caelo	Oak bark, cut	13360303	1
Caelo	Oak bark, cut	13360306	1
Caelo	Oak bark, cut	15314905	2
Caelo	Oak bark, cut	12221104	2
Caelo	Oak bark, cut	11351205	3
Caelo	Oak bark, cut	11351208	3
Euro OTC	Oak bark, cut		1
Galke	Oak bark, cut	17824	2
GEHE 10.03.2014	Oak bark, cut	761A11816	1
Gutenberg-Apotheke	Oak bark, cut	11351206	13
Caelo	Oak bark, cut	11351209	10
Klenk	Oak bark, cut	C-280513-2	1
Klenk	Oak bark, cut	761A110816	1
Klenk	Oak bark, cut	761A090420	1
Klenk	Oak bark, cut	761A110816	10
Noweda	Oak bark, cut	10348617	8
Caelo	Oak bark, cut	11351207	11
Klenk	Oak bark, cut	761A110816	1
Caelo	Oak bark, cut	12221105	2
Caelo	Oak bark, cut	13360302	6
Phönix	Oak bark, cut	10348609	2
Caelo	Oak bark, powdered	10261513	1
Caelo	Oat straw, cut	11280008	2
Caelo	Oat straw, cut	11280014	1
Caelo	Oat straw, cut	11280012	2
Caelo	Oat straw, cut	11280015	3
Caelo	Oat straw, cut	11280017	2
Noweda	Oat straw, cut	11280003	1
Caelo	Olive leaf	12159805	1
Caelo	Olive leaf	18100501	1
Klenk	Olive leaf	2211B131025	1
Klenk	Olive leaf	2211B130425	3
Klenk	Olive leaf	2211B120417	2
Klenk	Olive leaf	2211B150818	1
Klenk	Orange peel, cut	531A091125	3
Klenk	Orange peel, cut	531A130204	5
Klenk	Orange peel, cut	531a130204	1
Caelo	Oregano herb	12360904	1
Caelo	Oregano herb	11340705	1
Caelo	Oregano herb	11340708	1
Caelo	Oregano herb	11340709	1
Caelo	Oregano herb	12360901	6
Caelo	Oregano herb	11340703	2

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continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Oregano herb	12360902	3
Klenk	Oregano herb	4221A120315	2
Caelo	Orris root	11026704	2
Caelo	Orris root	11026706	1
Caelo	Orris root	13113401	2
Caelo	Orris root	1026706	1
Caelo	Orris root	13113404	1
Fagron	Orris root	11026705	3
Galke	Orris root	21303	1
Klenk	Orris root	B111013	1
Klenk	Orris root	6831B111013	1
Klenk	Orris root	B130102	1
Sanacorp	Orris root	11026701	1
Caelo	Orris root	13113402	1
Caelo	Oxycodone hydrochloride	17270202	2
Caelo	Parsley herb, rubbed	12376601	2
Caelo	Parsley herb, rubbed	51978126	1
Caelo	Parsley herb, rubbed	12376603	2
Caelo	Parsley herb, rubbed	12376602	2
Caelo	Parsley root, cut	12080309	1
Caelo	Parsley root, cut	12080304	1
Caelo	Parsley root, cut	13156003	1
Caelo	Parsley root, cut	13156005	1
Gahlke	Parsley root, cut	20872	1
Gehe	Parsley root, cut	6441A110210	3
Klenk	Parsley root, cut	6441A150811	1
Klenk	Parsley root, cut	6441A120606	5
Klenk	Parsley root, cut	6441A121024	4
Klenk	Parsley root, cut	6441A120283	1
Caelo	Parsley seed	PrüfNr. 2814A-01550	1
Klenk	Parsley seed	7370A091120	2
Klenk	Parsley seed	7370A09120	1
an	Passionflower herb, cut	13141212	1
Anzag	Passionflower herb, cut	1207211669	1
Caelo	Passionflower herb, cut	11049116	4
Caelo	Passionflower herb, cut	12031703	2
Caelo	Passionflower herb, cut	12031704	1
Caelo	Passionflower herb, cut	11049108	1
Caelo	Passionflower herb, cut	1011A-01669	1
Caelo	Passionflower herb, cut	12031701	1
Caelo	Passionflower herb, cut	12031715	7
Caelo	Passionflower herb, cut	12031716	3
Caelo	Passionflower herb, cut	12031712	1
Caelo	Passionflower herb, cut	12101301	1
Caelo	Passionflower herb, cut	13141201	1
Caelo	Passionflower herb, cut	15085105	1
Caelo	Passionflower herb, cut	12031706	3
Caelo	Passionflower herb, cut	11049111	1
Caelo	Passionflower herb, cut	13141202	6
Caelo	Passionflower herb, cut	12031710	13
Caelo	Passionflower herb, cut	12031705	4
Caelo	Passionflower herb, cut	13141205	4
Caelo	Passionflower herb, cut	12031714	2
Caelo	Passionflower herb, cut	12031717	9
Caelo	Passionflower herb, cut	13141203	2
Klenk	Passionflower herb, cut	4231A120329	2
Klenk	Passionflower herb, cut	A120329	2
Klenk	Passionflower herb, cut	4231A-110913	1
Klenk	Peony root, cut	B110916	2
Klenk	Peony root, cut	6421B120327	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Bombastus	Peppermint leaf, cut	266772	2
Bombastus	Peppermint leaf, cut	275295	3
Bombastus	Peppermint leaf, cut	246514	1
Bombastus	Peppermint leaf, cut	272956	3
Bombastus	Peppermint leaf, cut	279634	1
Bombastus	Peppermint leaf, cut	279214	1
Bombastus	Peppermint leaf, cut	281282	1
Bombastus	Peppermint leaf, cut	281043	3
Bombastus	Peppermint leaf, cut	271499	1
Bombastus	Peppermint leaf, cut	285914	1
Bombastus	Peppermint leaf, cut	276514	1
Bombastus	Peppermint leaf, cut	278679	2
Bombastus	Peppermint leaf, cut	279914	2
Bombastus	Peppermint leaf, cut	255719	1
Bombastus	Peppermint leaf, cut	282509	1
Caelo	Peppermint leaf, cut	20061202	1
Caelo	Peppermint leaf, cut	11327803	5
Caelo	Peppermint leaf, cut	20111215	1
Caelo	Peppermint leaf, cut	11294409	2
Caelo	Peppermint leaf, cut	11327801	2
Caelo	Peppermint leaf, cut	1132803	1
Caelo	Peppermint leaf, cut	12266903	5
Caelo	Peppermint leaf, cut	12266908	7
Caelo	Peppermint leaf, cut	2181B090928	1
Caelo	Peppermint leaf, cut	13030805	5
Caelo	Peppermint leaf, cut	Int.Ch.:313011	1
Caelo	Peppermint leaf, cut	ChB:311092	1
Caelo	Peppermint leaf, cut	13030806	1
Caelo	Peppermint leaf, cut	5091307	1
Caelo	Peppermint leaf, cut	13030809	2
Caelo	Peppermint leaf, cut	13030808	1
Caelo	Peppermint leaf, cut	8101301	1
Caelo	Peppermint leaf, cut	12032311	1
Caelo	Peppermint leaf, cut	13030804	1
Caelo	Peppermint leaf, cut	161212	1
Caelo	Peppermint leaf, cut	12266912	1
Caelo	Peppermint leaf, cut	13214706	1
Caelo	Peppermint leaf, cut	6011403	1
Caelo	Peppermint leaf, cut	13214720	1
Caelo	Peppermint leaf, cut	14083102	2
Caelo	Peppermint leaf, cut	14221701	1
Caelo	Peppermint leaf, cut	14339202	2
Caelo	Peppermint leaf, cut	13214707	3
Caelo	Peppermint leaf, cut	268320	1
Caelo	Peppermint leaf, cut	12054149	1
Caelo	Peppermint leaf, cut	13030807	3
Caelo	Peppermint leaf, cut	11294401	3
Caelo	Peppermint leaf, cut	13214705	1
Caelo	Peppermint leaf, cut	12266904	3
Caelo	Peppermint leaf, cut	11347609	1
Caelo	Peppermint leaf, cut	2181A1209-13	1
Caelo	Peppermint leaf, cut	12032319	2
Caelo	Peppermint leaf, cut	13105001	1
Caelo	Peppermint leaf, cut	13030808-3401310161	1
Caelo	Peppermint leaf, cut	12266908-343431160	1
Caesar & Loretz GmbH	Peppermint leaf, cut	11294411	1
Fagron	Peppermint leaf, cut	1234567	2
Fagron	Peppermint leaf, cut	13030803	3
Fiebig ek:9.84EUR 24.09...	Peppermint leaf, cut	2181A110512	5
Galke	Peppermint leaf, cut	22218	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Galke	Peppermint leaf, cut	20975	3
Galke	Peppermint leaf, cut	22783	3
Gehe	Peppermint leaf, cut	2181B130717A	1
Gehe	Peppermint leaf, cut	2181B130717B	1
Caelo	Peppermint leaf, cut	12266913	9
Hepart AG	Peppermint leaf, cut	B-185	5
HiperScan	Peppermint leaf, cut		1
Klenk	Peppermint leaf, cut	1209211505	1
Klenk	Peppermint leaf, cut	2181A-101013	1
Klenk	Peppermint leaf, cut	1001311505	1
Klenk	Peppermint leaf, cut	2161A110207	1
Klenk	Peppermint leaf, cut	1913A-01505	1
Klenk	Peppermint leaf, cut	2161A121009	6
Klenk	Peppermint leaf, cut	2183A120913	2
Klenk	Peppermint leaf, cut	2161A120718	3
Klenk	Peppermint leaf, cut	2181A130320	6
Klenk	Peppermint leaf, cut	216A121029	1
Klenk	Peppermint leaf, cut	2161A121206	14
Klenk	Peppermint leaf, cut	2161	1
Klenk	Peppermint leaf, cut	A121009	1
Klenk	Peppermint leaf, cut	2161A111207	1
Klenk	Peppermint leaf, cut	A130806	1
Klenk	Peppermint leaf, cut	2181B130717	10
Klenk	Peppermint leaf, cut	CH.2161B080818	1
Klenk	Peppermint leaf, cut	2161A130806	7
Klenk	Peppermint leaf, cut	2181A13020	1
Klenk	Peppermint leaf, cut	2161B140321	1
Klenk	Peppermint leaf, cut	2181A151119	1
Klenk	Peppermint leaf, cut	2181a120913	3
Klenk	Peppermint leaf, cut	4513E1503	1
Klenk	Peppermint leaf, cut	2161A07020203	1
Klenk	Peppermint leaf, cut	2181A-120913	1
Klenk	Peppermint leaf, cut	2181A100323	1
Klenk	Peppermint leaf, cut	2181A120913	34
Klenk	Peppermint leaf, cut	4113Q1505	1
Klenk	Peppermint leaf, cut	2161A121029	17
Klenk	Peppermint leaf, cut	2161A-121206	1
Kräuter-Schulte	Peppermint leaf, cut	56254	1
nachprüfung	Peppermint leaf, cut	C1327	1
Noweda	Peppermint leaf, cut	2911U-01505	1
Bombastus	Peppermint leaf, cut	273843	2
Klenk	Peppermint leaf, cut	2181A101013	6
Phönix	Peppermint leaf, cut	11327808	2
Probe	Peppermint leaf, cut	1223456	1
Wolf	Peppermint leaf, cut	P221379	7
Wolf	Peppermint leaf, cut	B-120	1
Wolf	Peppermint leaf, cut	B243	1
Wolf	Peppermint leaf, cut	B-725	2
Wolf	Peppermint leaf, cut	B725	1
BLS	Phenobarbital	67056	5
Fagron	Phenobarbital	13G05-N09	1
Fagron	Phenobarbital	15G07-B06-311718	1
Fagron	Phenobarbital	16G20-B04-328344	2
Fagron	Phenobarbital	18C07-B01-347288	1
Fagron	Phenobarbital	18H15-B01-354934	1
Th. Geyer	Phenobarbital	70510	2
Th. Geyer	Phenobarbital	67045	2
Caelo	Phenol	11163802	1
Caelo	Phenol	11163801	1
Caelo	Phenol	11163809	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Phenol	7061305	1
Caelo	Phenol	12223014	1
Caelo	Phenol	12223020	1
Caelo	Phenol	12223022	1
Caelo	Phenol	12223001	1
Caelo	Piper cubeba	11081903	1
Caelo	Podophyllum resin (fr...	11085807	4
Caelo	Podophyllum resin (fr...	12287805	1
Caelo	Podophyllum resin (fr...	11085811	1
Caelo	Podophyllum resin (fr...	12379903	1
Caelo	Podophyllum resin (fr...	12287810	1
Caelo	Podophyllum resin (fr...	82433349	1
Caelo	Potassium hydrocarbon...	12141924	3
Caelo	Potassium hydrocarbon...	11105808	1
Caelo	Potassium hydrocarbon...	11105812	1
Caelo	Potassium hydrocarbon...	11105804	1
Caelo	Potassium hydrocarbon...	11105818	1
Caelo	Potassium hydrocarbon...	12239702	2
Caelo	Potassium hydrocarbon...	8101202	1
Caelo	Potassium hydrocarbon...	1011M-01728	1
Caelo	Potassium hydrocarbon...	10052610	1
Caelo	Potassium hydrocarbon...	10052622	1
Caelo	Potassium hydrocarbon...	20080410-3	1
Caelo	Potassium hydrocarbon...	12141905	3
Caelo	Potassium hydrocarbon...	12239703	3
Caelo	Potassium hydrocarbon...	12141912	3
Caelo	Potassium hydrocarbon...	24051301	1
Caelo	Potassium hydrocarbon...	10052629	1
Caelo	Potassium hydrocarbon...	12141915	4
Caelo	Potassium hydrocarbon...	IntCh:217002	1
Caelo	Potassium hydrocarbon...	12141920	1
Caelo	Potassium hydrocarbon...	1214190	1
Caelo	Potassium hydrocarbon...	12141919	5
Caelo	Potassium hydrocarbon...	6011405	1
Caelo	Potassium hydrocarbon...	1214924	1
Caelo	Potassium hydrocarbon...	13390307	1
Caelo	Potassium hydrocarbon...	13141926	1
Caelo	Potassium hydrocarbon...	11105811	3
Caelo	Potassium hydrocarbon...	1303002-01	5
Caelo	Potassium hydrocarbon...	700544	1
Caelo	Potassium hydrocarbon...	3812Q-01728	1
Caelo	Potassium hydrocarbon...	13390303	1
Caelo	Potassium hydrocarbon...	12141930	2
Caelo	Potassium hydrocarbon...	12141910	8
Euro OTC	Potassium hydrocarbon...	1208010-01	3
Euro OTC	Potassium hydrocarbon...	1202013-01	1
Euro OTC	Potassium hydrocarbon...	4413I1728	1
Euro OTC	Potassium hydrocarbon...	1204038-01	2
Euro OTC	Potassium hydrocarbon...	2809033-01	1
Fagron	Potassium hydrocarbon...	12K27-N06	1
Fagron	Potassium hydrocarbon...	13031205	1
Fagron	Potassium hydrocarbon...	12141911	1
Noweda	Potassium hydrocarbon...	1004019-01	1
Caelo	Potassium hydrocarbon...	11105822	1
Caelo	Potassium hydrocarbon...	12239701	3
Fagron	Potassium hydrocarbon...	120801001	1
Caelo	Potassium hydroxide	12057905	1
Caelo	Potassium hydroxide	11165708	1
Caelo	Potassium hydroxide	17091202	1
Caelo	Potassium hydroxide	12057912	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Potassium hydroxide	12057908	2
Caelo	Potassium hydroxide	12057906	1
Caelo	Potassium hydroxide	12382606	2
Caelo	Potassium hydroxide	11165705	1
Caelo	Potassium hydroxide	12382611	1
Caelo	Potassium hydroxide	27111310	1
Caelo	Potassium hydroxide	13275201	2
Caelo	Potassium hydroxide	12382601	2
Caelo	Potassium hydroxide	13275207	1
Caesar & Loretz GmbH ...	Potassium hydroxide	12057902	2
Caelo	Potassium hydroxide	12382603	4
Fagron	Prednisolone 1:10 (ri...	12D04-N01	1
Fagron	Prednisolone 1:10 (ri...	12L19-N06	1
Aurica / 11	Primrose flower	521301234	1
Aurica/Gehe	Primrose flower	521203308	1
Caelo	Primrose flower	11206810	5
Caelo	Primrose flower	11206808	1
Caelo	Primrose flower	5021303	1
Caelo	Primrose flower	9021301	1
Caelo	Primrose flower	11206811	1
Caelo	Primrose flower	11374403	1
Caelo	Primrose flower	25091306	1
Caelo	Primrose flower	11206807	1
Caelo	Primrose flower	1308660	1
Caelo	Primrose flower	13086608	1
Caelo	Primrose flower	13276904	1
Caelo	Primrose flower	13086603	5
Caelo	Primrose flower	11374404	1
Caelo	Primrose flower	113744044	1
Caelo	Primrose flower	11374402	1
Caelo	Primrose flower	11374401	10
Caelo	Primrose flower	13086603	1
Caelo	Primrose flower	13086602	5
Caelo	Primrose flower	10207104	1
Caelo	Primrose flower	11206803	4
Caelo	Primrose flower	11206804	1
Caelo	Primrose flower	10072509	1
Galke	Primrose flower	22612	2
Gehe	Primrose flower	11374401	1
Caelo	Primrose flower	13086605	1
Klenk	Primrose flower	1541B100414	1
Klenk	Primrose flower	B110314	1
Klenk	Primrose flower	B130808	1
Klenk	Primrose flower	A111018	1
Klenk	Primrose flower	B130808	1
Klenk	Primrose flower	1540A-100907	1
Klenk	Primrose flower	1540A100907	1
Klenk	Primrose flower	1541B110314	7
Caelo	Primrose flower	11206811	4
Caelo	Primrose flower	11374403	3
Sanacorp	Primrose flower	1541B130808	6
Caelo	Primrose flower	13086602	3
VDL	Primrose flower	11206806	1
Weltecke / GEHE	Primrose flower	63011112	1
Caelo	Primrose root, cut	13087005	3
Caelo	Primrose root, cut	10382009	1
Caelo	Primrose root, cut	10382013	1
Caelo	Primrose root, cut	12064503	1
Caelo	Primrose root, cut	10382012	1
Caelo	Primrose root, cut	12064506	4

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Primrose root, cut	24011301	1
Caelo	Primrose root, cut	5010E-02159	1
Caelo	Primrose root, cut	Int.Ch:318090	1
Caelo	Primrose root, cut	13087004	1
Caelo	Primrose root, cut	4021410	1
Caelo	Primrose root, cut	10382010	1
Caelo	Primrose root, cut	13067001	1
Caelo	Primrose root, cut	13087001	1
Caelo	Primrose root, cut	71653517	1
Caelo	Primrose root, cut	13087005-3534411072	1
Caelo	Primrose root, cut	13087002	4
Klenk	Primrose root, cut	6461A100511	1
Klenk	Primrose root, cut	B130218	3
Noweda	Primrose root, cut	12064504	4
Audor Pharma	Psyllium seed	15190313	2
Bahnhof-Apotheke	Psyllium seed	3-121005	1
Caelo	Psyllium seed	10291205	1
Caelo	Psyllium seed	12140301	7
Caelo	Psyllium seed	10291206	1
Caelo	Psyllium seed	12185504	10
Caelo	Psyllium seed	10291204	1
Caelo	Psyllium seed	12185509	5
Caelo	Psyllium seed	12185508	4
Caelo	Psyllium seed	12276510	1
Caelo	Psyllium seed	13305904	2
Caelo	Psyllium seed	13305903	1
Caelo	Psyllium seed	13305906	2
Caelo	Psyllium seed	13305910	4
Caelo	Psyllium seed	10061503	1
Caelo	Psyllium seed	15190304	3
Caelo	Psyllium seed	10291207	6
Caelo	Psyllium seed	13234310	3
Caelo	Psyllium seed	12185503	3
Caelo	Psyllium seed	13234309	1
Caelo	Psyllium seed	7380a120911	1
Caelo	Psyllium seed	11185811	4
Caelo	Psyllium seed	15190303	4
Caelo	Psyllium seed	11185803	1
Caelo	Psyllium seed	13305907	5
Caelo	Psyllium seed	15190306	1
Caelo	Psyllium seed	12185502	1
Caesar/Noweda	Psyllium seed	11185817	3
Caesar/Noweda	Psyllium seed	12276501	3
Galke	Psyllium seed	20968	2
Galke	Psyllium seed	22989	7
Klenk	Psyllium seed	7380A150520	7
Klenk	Psyllium seed	7560a120330	1
Klenk	Psyllium seed	A120911	1
Klenk	Psyllium seed	A120109	1
Klenk	Psyllium seed	A130128	1
Klenk	Psyllium seed	7560A130418	1
Klenk	Psyllium seed	7380A150929	4
Klenk	Psyllium seed	7380A161018	2
Klenk	Psyllium seed	7380A110317	1
Klenk	Psyllium seed	7380A111018	1
Klenk	Psyllium seed	7380A130128	6
Klenk	Psyllium seed	7380A120109	24
Klenk	Psyllium seed	7380a111018	1
Klenk	Psyllium seed	7380a120109	3
Klenk	Psyllium seed	7380A120911	16

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Psyllium seed	7560A140203	1
Allianz Healthcare	Pumpkin seed, peeled	16081210	1
Caelo	Pumpkin seed, peeled	12249001	2
Caelo	Pumpkin seed, peeled	14186905	1
Caelo	Pumpkin seed, peeled	14186910	1
Caelo	Pumpkin seed, peeled	16081202	1
Caelo	Pumpkin seed, peeled	16081206	2
Caelo	Pumpkin seed, peeled	140736306	1
Caelo	Pumpkin seed, peeled	122490911	1
Caelo	Pumpkin seed, peeled	12249011	2
Caelo	Pumpkin seed, peeled	14073603	1
sanacorp	Pumpkin seed, peeled	14186909	1
Sanacorp	Pumpkin seed, peeled	16081212	1
Caelo	Ramsons herb, cut	11182207	1
Caelo	Ramsons herb, cut	11182204	1
Caelo	Ramsons herb, cut	11182203	1
Caelo	Ramsons herb, cut	12380802	2
Caelo	Ramsons herb, cut	12380801	2
Caelo	Ramsons herb, cut	12380803	1
Caelo	Ramsons herb, cut	14343305	1
Klenk	Ramsons herb, cut	3511B111005	2
-	Raspberry leaf, cut	130849	1
Alfred Galke	Raspberry leaf, cut	19851	1
an	Raspberry leaf, cut	13086708	1
Anzag	Raspberry leaf, cut	2291A120806	2
Anzag	Raspberry leaf, cut	12103107	11
Anzag ek:3,00EUR 11.09.12	Raspberry leaf, cut	12103105	18
Caelo	Raspberry leaf, cut	1236705	1
Caelo	Raspberry leaf, cut	10136412	1
Klenk	Raspberry leaf, cut	2291A120507	5
Bahnhof-Apotheke	Raspberry leaf, cut	17-120917	1
Bombastus	Raspberry leaf, cut	274507	1
Bombastus	Raspberry leaf, cut	279686	3
Bombastus	Raspberry leaf, cut	273668	2
Bombastus	Raspberry leaf, cut	269870	1
Bombastus	Raspberry leaf, cut	273778	1
Bombastus	Raspberry leaf, cut	272898	1
Bombastus	Raspberry leaf, cut	248586	1
Bombastus	Raspberry leaf, cut	267122	1
Caelo	Raspberry leaf, cut	1310603	1
Caelo	Raspberry leaf, cut	10013407	1
Caelo	Raspberry leaf, cut	307211511	1
Caelo	Raspberry leaf, cut	10013411	1
Caelo	Raspberry leaf, cut	9081205	1
Caelo	Raspberry leaf, cut	22081201	1
Caelo	Raspberry leaf, cut	25091201	1
Caelo	Raspberry leaf, cut	2909211511	1
Caelo	Raspberry leaf, cut	9101204	1
Caelo	Raspberry leaf, cut	18101203	1
Caelo	Raspberry leaf, cut	12103108	8
Caelo	Raspberry leaf, cut	11121201	1
Caelo	Raspberry leaf, cut	12103109	2
Caelo	Raspberry leaf, cut	17121203	1
Caelo	Raspberry leaf, cut	1210315	1
Caelo	Raspberry leaf, cut	12362702	7
Caelo	Raspberry leaf, cut	8031307	1
Caelo	Raspberry leaf, cut	10013410	1
Caelo	Raspberry leaf, cut	18041304	1
Caelo	Raspberry leaf, cut	12362706	29
Caelo	Raspberry leaf, cut	11030706	3

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Raspberry leaf, cut	21051302	1
Caelo	Raspberry leaf, cut	IntCh:311090	1
Caelo	Raspberry leaf, cut	11071301	1
Caelo	Raspberry leaf, cut	20081311	1
Caelo	Raspberry leaf, cut	12362707	4
Caelo	Raspberry leaf, cut	13038002	1
Caelo	Raspberry leaf, cut	13038003	1
Caelo	Raspberry leaf, cut	13101803	1
Caelo	Raspberry leaf, cut	12362711	9
Caelo	Raspberry leaf, cut	12362708	4
Caelo	Raspberry leaf, cut	10136408	1
Caelo	Raspberry leaf, cut	7011402	1
Caelo	Raspberry leaf, cut	9011404	1
Caelo	Raspberry leaf, cut	13127901	3
Caelo	Raspberry leaf, cut	30011408	1
Caelo	Raspberry leaf, cut	14018803	1
Caelo	Raspberry leaf, cut	12103101	7
Caelo	Raspberry leaf, cut	2271C120508	5
Caelo	Raspberry leaf, cut	12362704	5
Caelo	Raspberry leaf, cut	713E-01511	1
Caelo	Raspberry leaf, cut	11030707	3
Caelo	Raspberry leaf, cut	12362705	9
Caelo	Raspberry leaf, cut	314U1511	1
Caelo	Raspberry leaf, cut	12392709	1
Caelo	Raspberry leaf, cut	6859427	1
Caelo	Raspberry leaf, cut	12368706	1
Caelo	Raspberry leaf, cut	12362709	7
Caelo	Raspberry leaf, cut	231013c	1
Caelo	Raspberry leaf, cut	10136404	1
Caelo	Raspberry leaf, cut	12362710	14
Caelo	Raspberry leaf, cut	12362710-3432311160	1
Caelo	Raspberry leaf, cut	13101604	3
Caelo	Raspberry leaf, cut	13101602-347312141	1
Caesar & Loretz GmbH,...	Raspberry leaf, cut	10013408	1
China Medica	Raspberry leaf, cut	13086703	1
Galke	Raspberry leaf, cut	21244	1
Galke	Raspberry leaf, cut	18060	2
Galke	Raspberry leaf, cut	19499	2
Galke	Raspberry leaf, cut	23532	1
gehe 10.12.13	Raspberry leaf, cut	229117121120	1
Gutenberg-Apotheke	Raspberry leaf, cut	28911	1
Klenk	Raspberry leaf, cut	2291A12112o	1
Caelo	Raspberry leaf, cut	11030705	1
Caelo	Raspberry leaf, cut	13101605	1
Kenk / Phoenix	Raspberry leaf, cut	22781C120508	1
Klenk	Raspberry leaf, cut	2291A-120806	1
Klenk	Raspberry leaf, cut	12273107	1
Klenk	Raspberry leaf, cut	2291A130320	1
Klenk	Raspberry leaf, cut	A130430	1
Klenk	Raspberry leaf, cut	2291A121120	4
Klenk	Raspberry leaf, cut	2291A120813	2
Klenk	Raspberry leaf, cut	2291a111124	1
Klenk	Raspberry leaf, cut	2291A110125	1
Phoenix	Raspberry leaf, cut	10136409	1
Caelo	Raspberry leaf, cut	12130107	1
Phönix	Raspberry leaf, cut	12362701	7
Caelo	Raspberry leaf, cut	12103111	15
Klenk	Raspberry leaf, cut	2291A111124	1
Sanacorp	Raspberry leaf, cut	12362703	9
Sanacorp	Raspberry leaf, cut	13038001	6

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Raspberry leaf, cut	10013409	2
Caelo	Raspberry leaf, cut	13101603	5
Caelo	Raspberry leaf, cut	11030704	2
VDL	Raspberry leaf, cut	10013406	3
Wolf	Raspberry leaf, cut	P201727	19
Wolf	Raspberry leaf, cut	P222676	1
Wolf	Raspberry leaf, cut	B-457	1
Aurica	Red clover flower	521206331	1
Aurica	Red clover flower	521203442	1
Aurica/Anzag	Red clover flower	521303918	1
Galke	Red clover flower	23128	2
Klenk	Red clover flower	7470A130311	1
Klenk	Red clover flower	811Q-07163	1
Klenk	Red clover flower	1640A110727	1
Klenk	Red clover flower	1640a130122	1
Klenk	Red clover flower	1640A130122	15
Kräuter Schulte	Red clover flower	53778	1
Caelo	Red poppy petals, cut	12330205	1
Kräuter Schulte	Red tea	52029	1
Caelo	Red-rose petal	12380008	2
Galke	Red-rose petal	22641	2
Klenk	Red-rose petal	1561A121016	1
Caelo	Red-rose petal	12380004	1
Klenk	Red-rose petal, cut	1561A110404	1
Caelo	Red-rose petal, cut	10306514	1
Caelo	Red-rose petal, cut	11304901	3
Caelo	Red-rose petal, cut	11304906	1
Caelo	Red-rose petal, cut	11304904	4
Caelo	Red-rose petal, cut	11011301	1
Caelo	Red-rose petal, cut	12380001	4
Caelo	Red-rose petal, cut	11304912	2
Caelo	Red-rose petal, cut	12380008	1
Caelo	Red-rose petal, cut	13194403	4
Caelo	Red-rose petal, cut	10113211	1
Caelo	Red-rose petal, cut	12380007-3357319071	1
Caelo	Red-rose petal, cut	12380004	2
Caelo	Red-rose petal, cut	13194402	1
Klenk	Red-rose petal, cut	1561B101210	2
Klenk	Red-rose petal, cut	1561A121016-34023101	1
kräuter schulte	Red-rose petal, cut	47543	1
Richter	Red-rose petal, cut	P236157	1
Caelo	Redwood	12049608	2
Caelo	Redwood	12041403	1
Caelo	Redwood	13106901	1
Caelo	Redwood	12049607	2
Klenk	Redwood	5961B111219	1
Caelo	Restharrow root, cut	71035467	1
Bombastus	Restharrow root, cut	274421	1
Bombastus	Restharrow root, cut	272831	2
Bombastus	Restharrow root, cut	283708	1
Caelo	Restharrow root, cut	11247302	2
Caelo	Restharrow root, cut	11103105	2
Caelo	Restharrow root, cut	6101201	1
Caelo	Restharrow root, cut	20111213	1
Caelo	Restharrow root, cut	21011306	1
Caelo	Restharrow root, cut	12330001	14
Caelo	Restharrow root, cut	12330001	2
Caelo	Restharrow root, cut	Int.Ch:212150	1
Caelo	Restharrow root, cut	12330005	5
Caelo	Restharrow root, cut	15101313	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Restharrow root, cut	4021406	1
Caelo	Restharrow root, cut	12330002	1
Caelo	Restharrow root, cut	12330003	2
Caelo	Restharrow root, cut	1230004	1
Caelo	Restharrow root, cut	72439069	1
Caesar/Noweda	Restharrow root, cut	71015/3	2
Galke	Restharrow root, cut	12700	1
Hepart AG	Restharrow root, cut	B130404	3
Klenk	Restharrow root, cut	6411111110	1
Klenk	Restharrow root, cut	6411B101216	2
Klenk	Restharrow root, cut	4296345	1
Klenk	Restharrow root, cut	6411B111110	1
Klenk	Restharrow root, cut	B111110	1
Klenk	Restharrow root, cut	6411B130404	2
Caelo	Restharrow root, cut	11103107	2
Caelo	Rhubarb, cut	11265902	1
Caelo	Rhubarb, cut	11057810	1
Caelo	Rhubarb, cut	12211903	4
Caelo	Rhubarb, cut	11057818	2
Caelo	Rhubarb, cut	10071302	1
Caelo	Rhubarb, cut	12211908	1
Caelo	Rhubarb, cut	11321806	1
Caelo	Rhubarb, cut	15101301	1
Caelo	Rhubarb, cut	13235201	2
Caelo	Rhubarb, cut	25111305	1
Caelo	Rhubarb, cut	14155404	1
Caelo	Rhubarb, cut	12211904	2
Caelo	Rhubarb, cut	12211902	3
Caelo	Rhubarb, cut	13235205	1
Caelo	Rhubarb, cut	11057804	1
Caelo	Rhubarb, cut	12211906	1
Caelo	Rhubarb, cut	13235203	1
Gehe	Rhubarb, cut	13235208	2
Klenk	Rhubarb, cut	6891B111118	1
Klenk	Rhubarb, cut	7761B130514	2
Phoenix	Rhubarb, cut	11057817	3
Phönix	Rhubarb, cut	12211905	3
vedono	Rhubarb, cut	12211907	6
Bombastus	Rhubarb, powdered	11043806	1
Caelo	Rhubarb, powdered	11043819	2
Caelo	Rhubarb, powdered	9071201	1
Caelo	Rhubarb, powdered	11043817	1
Caelo	Rhubarb, powdered	11043818	1
Caelo	Rhubarb, powdered	11043816	1
Caelo	Rhubarb, powdered	11043826	1
Caelo	Rhubarb, powdered	13193106	2
Caelo	Rhubarb, powdered	23061402	1
Caelo	Rhubarb, powdered	11043809	1
Caelo	Rhubarb, powdered	11043816	2
Caelo	Rhubarb, powdered	11043818	1
Caelo	Rhubarb, powdered	11043825	2
Caelo	Rhubarb, powdered	11043822	1
Caelo	Rhubarb, powdered	13193104	4
Caelo	Rhubarb, powdered	13193109	1
Fagron	Rhubarb, powdered	11043821	1
Hedinger	Rhubarb, powdered	13193110	1
Caelo	Ribwort plantain, cut	13113007	6
Bahnhof-Apotheke	Ribwort plantain, cut	7-121011	1
Bombastus	Ribwort plantain, cut	276453	1
Bombastus	Ribwort plantain, cut	275479	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Ribwort plantain, cut	13113008	5
Caelo	Ribwort plantain, cut	23121304	1
Caelo	Ribwort plantain, cut	10315707	2
Caelo	Ribwort plantain, cut	8061208	1
Caelo	Ribwort plantain, cut	17071201	1
Caelo	Ribwort plantain, cut	10315715	9
Caelo	Ribwort plantain, cut	10315712	2
Caelo	Ribwort plantain, cut	15101204	1
Caelo	Ribwort plantain, cut	10315711	4
Caelo	Ribwort plantain, cut	20111208	1
Caelo	Ribwort plantain, cut	12225802	5
Caelo	Ribwort plantain, cut	19121202	1
Caelo	Ribwort plantain, cut	12225804	1
Caelo	Ribwort plantain, cut	12362902	7
Caelo	Ribwort plantain, cut	22021302	1
Caelo	Ribwort plantain, cut	2031302	1
Caelo	Ribwort plantain, cut	12362906	7
Caelo	Ribwort plantain, cut	25041301	1
Caelo	Ribwort plantain, cut	13113001	8
Caelo	Ribwort plantain, cut	11061304	1
Caelo	Ribwort plantain, cut	28061301	1
Caelo	Ribwort plantain, cut	25091305	1
Caelo	Ribwort plantain, cut	1362903	1
Caelo	Ribwort plantain, cut	16101304	1
Caelo	Ribwort plantain, cut	13113005	5
Caelo	Ribwort plantain, cut	15111302	1
Caelo	Ribwort plantain, cut	20111304	1
Caelo	Ribwort plantain, cut	10011402	1
Caelo	Ribwort plantain, cut	13113010	4
Caelo	Ribwort plantain, cut	4021411	1
Caelo	Ribwort plantain, cut	13410603	3
Caelo	Ribwort plantain, cut	13410601	1
Caelo	Ribwort plantain, cut	13410612	1
Caelo	Ribwort plantain, cut	14199202	1
Caelo	Ribwort plantain, cut	15096301	1
Caelo	Ribwort plantain, cut	15096308	1
Caelo	Ribwort plantain, cut	13232401	1
Caelo	Ribwort plantain, cut	10315705	1
Caelo	Ribwort plantain, cut	1313007	1
Caelo	Ribwort plantain, cut	10315714	2
Caelo	Ribwort plantain, cut	10328702	2
Caelo	Ribwort plantain, cut	12225803	2
Caelo	Ribwort plantain, cut	12362903-3388311070	1
Caelo	Ribwort plantain, cut	13113004-3488312172	1
Caelo	Ribwort plantain, cut	13113006	6
Caesar & Loretz GmbH,...	Ribwort plantain, cut	12362903	33
Caesar & Loretz GmbH,...	Ribwort plantain, cut	13113004	13
Cealo	Ribwort plantain, cut	12362907	2
Galke	Ribwort plantain, cut	20259	1
Galke	Ribwort plantain, cut	21598	1
Gehe	Ribwort plantain, cut	1080413	1
Hepart AG	Ribwort plantain, cut	20832	5
Klenk	Ribwort plantain, cut	4271A130115	6
Klenk	Ribwort plantain, cut	4271A-110816	1
Klenk	Ribwort plantain, cut	A110816	1
Klenk	Ribwort plantain, cut	4271A130716	1
Klenk	Ribwort plantain, cut	4281N111121	1
Klenk	Ribwort plantain, cut	4271A111125	2
Klenk	Ribwort plantain, cut	4271A100615	2
Klenk	Ribwort plantain, cut	4271A110816	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Ribwort plantain, cut	427A111125	1
Phoenix	Ribwort plantain, cut	4271A11016	1
Sanacorp	Ribwort plantain, cut	263401	1
Caelo	Ribwort plantain, cut	12362901	1
C	Robert herb, cut	11147810	3
Caelo	Robert herb, cut	11147807	3
Caelo	Robert herb, cut	11147804	1
Caelo	Robert herb, cut	8121203	1
Caelo	Robert herb, cut	11147813	2
Caelo	Robert herb, cut	12319305	1
Caelo	Robert herb, cut	12319304	2
Caelo	Robert herb, cut	11147812	3
Caelo	Robert herb, cut	12319302	1
Klenk	Robert herb, cut	A110621	6
Klenk	Robert herb, cut	3951A110621	7
Klenk	Robert herb, cut	3951B121218	2
Klenk	Robert herb, cut	3951B12118	1
Caelo	Rose hips peel, cut	12064207	1
Bombastus	Rose hips peel, cut	275394	2
Bombastus	Rose hips peel, cut	283458	1
Bombastus	Rose hips peel, cut	257166	1
Bombastus	Rose hips peel, cut	277431	3
Bombastus	Rose hips peel, cut	285184	1
Bombastus	Rose hips peel, cut	231013A	1
Caelo	Rose hips peel, cut	15061210	1
Caelo	Rose hips peel, cut	25061203	1
Caelo	Rose hips peel, cut	11301405	2
Caelo	Rose hips peel, cut	10101206	1
Caelo	Rose hips peel, cut	11301401	1
Caelo	Rose hips peel, cut	7031305	1
Caelo	Rose hips peel, cut	12288301	1
Caelo	Rose hips peel, cut	12357501	1
Caelo	Rose hips peel, cut	12357505	6
Caelo	Rose hips peel, cut	5091301	1
Caelo	Rose hips peel, cut	12357504	2
Caelo	Rose hips peel, cut	9121301	1
Caelo	Rose hips peel, cut	14050704	1
Caelo	Rose hips peel, cut	14050705	1
Caelo	Rose hips peel, cut	2851A120904konv.	1
Caelo	Rose hips peel, cut	10157309	1
Caelo	Rose hips peel, cut	13317805	1
Caelo	Rose hips peel, cut	11301403	2
Caelo	Rose hips peel, cut	13317801	2
Caelo	Rose hips peel, cut	12357502	3
Klenk	Rose hips peel, cut	2851A150310	4
Klenk	Rose hips peel, cut	2851A101119	3
Klenk	Rose hips peel, cut	2851A110202	1
Klenk	Rose hips peel, cut	2841B111019	2
Klenk	Rose hips peel, cut	2851A120102	5
Klenk	Rose hips peel, cut	2851A120904	2
Klenk	Rose hips peel, cut	A120904	3
Klenk	Rose hips peel, cut	2851A-110202	1
Klenk	Rose hips peel, cut	3613M-01543	1
Caelo	Rose hips peel, cut	11301407	12
Caelo	Rose hips peel, cut	12288302	6
Aurica	Rose hips with peel, ...	521201801	1
Caelo	Rose hips with peel, ...	307211542	1
Caelo	Rose hips with peel, ...	16111201	1
Caelo	Rose hips with peel, ...	19111204	1
Caelo	Rose hips with peel, ...	12064207	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Rose hips with peel, ...	1512211542	1
Caelo	Rose hips with peel, ...	12064210	3
Caelo	Rose hips with peel, ...	2103311542	1
Caelo	Rose hips with peel, ...	12064209	4
Caelo	Rose hips with peel, ...	12029011	1
Caelo	Rose hips with peel, ...	12064213	1
Caelo	Rose hips with peel, ...	13048703	1
Caelo	Rose hips with peel, ...	13048704	1
Caelo	Rose hips with peel, ...	13048704	3
Caelo	Rose hips with peel, ...	12029008	1
Caelo	Rose hips with peel, ...	12064210	2
Caelo	Rose hips with peel, ...	12064212	3
Caelo	Rose hips with peel, ...	12064201	1
Caelo	Rose hips with peel, ...	12064209	1
Caelo	Rose hips with peel, ...	12064213	1
Caelo	Rose hips with peel, ...	13048703	1
Caelo	Rose hips with peel, ...	12064202	1
Caelo	Rose hips with peel, ...	12064207	3
Caelo	Rose hips with peel, ...	13048701	2
Caelo	Rose hips with peel, ...	114Q-01542	1
Caelo	Rose hips with peel, ...	13097405	1
Caelo	Rose hips with peel, ...	12064212	2
Klenk	Rose hips with peel, ...	B111019	1
Klenk	Rose hips with peel, ...	A120719	1
Klenk	Rose hips with peel, ...	B130523	1
Klenk	Rose hips with peel, ...	A120904	1
Klenk	Rose hips with peel, ...	2841B081210	1
Klenk	Rose hips with peel, ...	2841B111019	3
Klenk	Rose hips with peel, ...	3613M-01542	1
Klenk	Rose hips with peel, ...	2851A120904	1
Phönix	Rose hips with peel, ...	10281021	1
Phönix	Rose hips with peel, ...	2841B130523	1
Phönix	Rose hips with peel, ...	2841B130523	1
Caelo	Rose hips with peel, ...	12064202	1
Caelo	Rose hips with peel, ...	12064206	1
Caelo	Rose mallow flower, cut	13040402	1
Caelo	Rose mallow flower, cut	13040401	2
Caelo	Rose mallow flower, cut	10244507	1
an	Roselle	14018101	1
Caelo	Roselle	12267502	4
Caelo	Roselle	11036504	1
Caelo	Roselle	11036512	1
Caelo	Roselle	7121301	1
Caelo	Roselle	12267507	2
Caelo	Roselle	12267504	3
Caelo	Roselle	12007306	1
Caelo	Roselle	11036509	1
Caelo	Roselle	12267503	2
Caelo	Roselle	12267501	3
Caelo	Roselle	12267502	3
Caelo	Roselle	12267504	1
Caelo	Roselle	12267504-3428311150	1
Caelo	Roselle	11036511	1
Klenk	Roselle	1431B130205	1
Klenk	Roselle	B130205	1
Klenk	Roselle	1431B-110519	1
Klenk	Roselle	1431B131015	2
Klenk	Roselle	1431B111122	1
Sanacorp	Roselle	12267508	2
vedono	Roselle	12007313	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Akazie	Rosemary leaf, cut	20.09.2015	1
Bahnhof-Apotheke	Rosemary leaf, cut	7-120915	1
Bomastus-Werke/Phönix	Rosemary leaf, cut	298424	2
Bombastus	Rosemary leaf, cut	277128	1
Bombastus	Rosemary leaf, cut	281248	1
Bombastus	Rosemary leaf, cut	270171	1
Bombastus	Rosemary leaf, cut	281843	1
Caelo	Rosemary leaf, cut	11193402	2
Caelo	Rosemary leaf, cut	11193405	1
Caelo	Rosemary leaf, cut	11193404	1
Caelo	Rosemary leaf, cut	11193408	6
Caelo	Rosemary leaf, cut	5041302	1
Caelo	Rosemary leaf, cut	IntCh:313060	1
Caelo	Rosemary leaf, cut	12225902	1
Caelo	Rosemary leaf, cut	13128801	1
Caelo	Rosemary leaf, cut	13128802	2
Caelo	Rosemary leaf, cut	13128806	2
Caelo	Rosemary leaf, cut	13128805	1
Caelo	Rosemary leaf, cut	28051404	1
Caelo	Rosemary leaf, cut	14082901	1
Caelo	Rosemary leaf, cut	14159601	1
Caelo	Rosemary leaf, cut	1415901	1
Caelo	Rosemary leaf, cut	17352502	1
Caelo	Rosemary leaf, cut	11193406	1
Caelo	Rosemary leaf, cut	11193405	1
Caelo	Rosemary leaf, cut	15125001	2
Caelo	Rosemary leaf, cut	15125008	1
Galke	Rosemary leaf, cut	21390	1
Galke	Rosemary leaf, cut	19813	1
Galke	Rosemary leaf, cut	22777	1
Klenk	Rosemary leaf, cut	301401	1
Klenk	Rosemary leaf, cut	2261A120224	18
Klenk	Rosemary leaf, cut	A130201	2
Klenk	Rosemary leaf, cut		1
Klenk	Rosemary leaf, cut	61A131118	1
Klenk	Rosemary leaf, cut	2261A170803	1
Klenk	Rosemary leaf, cut	2261A140910	4
Klenk	Rosemary leaf, cut	2216A170803	1
Klenk	Rosemary leaf, cut	2261A130201	29
Klenk	Rosemary leaf, cut	2261A160329	2
Klenk	Rosemary leaf, cut	112E-01510	1
Klenk	Rosemary leaf, cut	2261A160905	4
Klenk	Rosemary leaf, cut	2261A150622	6
Klenk	Rosemary leaf, cut	2261A081117	1
Klenk	Rosemary leaf, cut	2261a160329	1
Klenk	Rosemary leaf, cut	2261A131118	12
Noweda	Rosemary leaf, cut	2261A100916	1
Noweda	Rosemary leaf, cut	15428011	1
Klenk	Rosemary leaf, cut	2261a120224	2
Klenk	Rosemary leaf, cut	2261A170317	1
Caelo	Rue herb, cut		1
Caelo	Rue herb, cut	9336802	1
Caelo	Rue herb, cut	12148804	1
Caelo	Rue herb, cut	12148806	1
Caelo	Rue herb, cut	12148801	1
Caelo	Rue herb, cut	11371803	1
Caelo	Rue herb, cut	12148803	2
Gehe	Rue herb, cut	12148802	1
Klenk	Rue herb, cut	A120207	1
Klenk	Rue herb, cut	4361A120207	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Rue herb, cut	4361A07020601	1
Klenk	Rue herb, cut	4361A100707	3
Fagron	Rutoside trihydrate	13K12-B06	1
Fagron	Rutoside trihydrate	13K12-B06295483	1
Fagron	Rutoside trihydrate	13K12B06295483	1
Fagron	Rutoside trihydrate	L14050127	1
Klenk	Saffron (spice)	384A110608	1
Klenk	Saffron (spice)	384A-120410	1
Klenk	Saffron (spice)	384A130320	2
Klenk	Saffron (spice)	384a120410	1
Caelo	Saffron filaments	10184811	2
Caelo	Saffron filaments	11071310	1
Caelo	Saffron filaments	15101305	1
Caelo	Saffron filaments	21011403	1
Caelo	Saffron filaments	12108311	2
Caelo	Saffron filaments	10184822	1
Caelo	Saffron filaments	12108308	2
Fagron	Saffron filaments	380A120416	1
Klenk	Saffron filaments	380A130613	1
Anzag ek: 3,06 11.09...	Sage leaf, cut	2301A120403	38
Aurica	Sage leaf, cut	521204613	1
Bahnhof-Apotheke	Sage leaf, cut	3-121018	1
Bombastus	Sage leaf, cut	270115	1
Bombastus	Sage leaf, cut	271253	1
Bombastus	Sage leaf, cut	277512	1
Bombastus	Sage leaf, cut	255381	1
Caelo	Sage leaf, cut	11056109	5
Caelo	Sage leaf, cut	22061201	1
Caelo	Sage leaf, cut	22081203	1
Caelo	Sage leaf, cut	31081202	1
Caelo	Sage leaf, cut	1209211513	1
Caelo	Sage leaf, cut	11056123	5
Caelo	Sage leaf, cut	410211513	1
Caelo	Sage leaf, cut	111012004	1
Caelo	Sage leaf, cut	11056125	3
Caelo	Sage leaf, cut	11347508	3
Caelo	Sage leaf, cut	12112101	1
Caelo	Sage leaf, cut	22111203	1
Caelo	Sage leaf, cut	15121201	1
Caelo	Sage leaf, cut	20121201	1
Caelo	Sage leaf, cut	11347511	9
Caelo	Sage leaf, cut	11347509	4
Caelo	Sage leaf, cut	12021302	1
Caelo	Sage leaf, cut	103311513	1
Caelo	Sage leaf, cut	12370001	18
Caelo	Sage leaf, cut	15041304	1
Caelo	Sage leaf, cut	11347513	1
Caelo	Sage leaf, cut	12370006	8
Caelo	Sage leaf, cut	17061302	1
Caelo	Sage leaf, cut	25061302	1
Caelo	Sage leaf, cut	312010	1
Caelo	Sage leaf, cut	26081301	1
Caelo	Sage leaf, cut	12370004	2
Caelo	Sage leaf, cut	14111315	1
Caelo	Sage leaf, cut	9121302	1
Caelo	Sage leaf, cut	12370015	2
Caelo	Sage leaf, cut	8011420	1
Caelo	Sage leaf, cut	13011405	1
Caelo	Sage leaf, cut	12370017	1
Caelo	Sage leaf, cut	13266603	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sage leaf, cut	13266605	3
Caelo	Sage leaf, cut	13266606	1
Caelo	Sage leaf, cut	13266621	1
Caelo	Sage leaf, cut	13266626	1
Caelo	Sage leaf, cut	12370013	3
Caelo	Sage leaf, cut	279939	1
Caelo	Sage leaf, cut	11347503	1
Caelo	Sage leaf, cut	12380009	1
Caelo	Sage leaf, cut	1237003	1
Caelo	Sage leaf, cut	123770010	1
Caelo	Sage leaf, cut	12370011	11
Caelo	Sage leaf, cut	12370003-3359319071	1
Caelo	Sage leaf, cut	12370014-3477312161	1
Caelo	Sage leaf, cut	12370014-3541411092	1
Caelo	Sage leaf, cut	12370014	8
Caelo	Sage leaf, cut	12370009	12
Caesar & Loretz GmbH ...	Sage leaf, cut	11056121	3
Caesar & Loretz GmbH,...	Sage leaf, cut	11347502	5
Caesar & Loretz GmbH,...	Sage leaf, cut	12370002	4
Caesar & Loretz GmbH,...	Sage leaf, cut	12370010	16
Caesar & Loretz GmbH,...	Sage leaf, cut	12370016	9
Finze	Sage leaf, cut	2301A110204	7
Galke	Sage leaf, cut	21015	3
gehe 07.12.2013	Sage leaf, cut	2301/7120403	1
Kenk / Phoenix	Sage leaf, cut	2301A130904	2
Klenk	Sage leaf, cut	C120126	1
Klenk	Sage leaf, cut	2301A110420	1
Klenk	Sage leaf, cut	2301C12126	1
Klenk	Sage leaf, cut	2301a120403	1
Klenk	Sage leaf, cut	2301c120126	1
Klenk	Sage leaf, cut	2301C12026	1
Klenk	Sage leaf, cut	2301C120126	16
Klenk	Sage leaf, cut	2301A110420	2
Nachprüfung 21.11.11	Sage leaf, cut	C1247	1
Phoenix	Sage leaf, cut	231C130326	1
Caelo	Sage leaf, cut	12370003	4
Wolf	Sage leaf, cut	B735	1
Noweda	Salbutamol sulfate	13K12-N02	1
Galke	Sanicle herb, cut	23097	1
Kräuter Schulte	Saponaria root, cut	54524	2
Kräuter Schulte	Saponaria root, cut	54977	1
Kräuter Schulte	Saponaria root, cut	54500	1
Caelo	Sarsaparilla root, cut	13079201	1
Klenk	Sarsaparilla root, cut	6561B111108	1
Klenk	Sarsaparilla root, cut	B111108	1
bohn	Savory, rubbed	12177208	1
Caelo	Savory, rubbed	12177203	7
Caelo	Savory, rubbed	12200801	1
Caelo	Savory, rubbed	12177201	1
Caelo	Savory, rubbed	12177207	2
Caelo	Savory, rubbed	13172404	2
Hepart AG	Savory, rubbed	12177205	3
Bomba/AHD	Senna leaf, cut	280008	1
Bombastus	Senna leaf, cut	280448	1
Bombastus	Senna leaf, cut	273547	3
Bombastus	Senna leaf, cut	278109	1
Bombastus	Senna leaf, cut	273474	1
Bombastus	Senna leaf, cut	280581	2
Caelo	Senna leaf, cut	11277304	4
Caelo	Senna leaf, cut	806211514	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Senna leaf, cut	11277305	1
Caelo	Senna leaf, cut	11277316	4
Caelo	Senna leaf, cut	18071201	1
Caelo	Senna leaf, cut	2909211514	1
Caelo	Senna leaf, cut	711211514	1
Caelo	Senna leaf, cut	1273103	1
Caelo	Senna leaf, cut	12273107	9
Caelo	Senna leaf, cut	103311514	2
Caelo	Senna leaf, cut	12273105	6
Caelo	Senna leaf, cut	1803311514	1
Caelo	Senna leaf, cut	11041009	1
Caelo	Senna leaf, cut	12273114	2
Caelo	Senna leaf, cut	2231B13014	1
Caelo	Senna leaf, cut	2413Q01514	1
Caelo	Senna leaf, cut	12115502	1
Caelo	Senna leaf, cut	9071302	1
Caelo	Senna leaf, cut	12276111	1
Caelo	Senna leaf, cut	313082	1
Caelo	Senna leaf, cut	5091306	1
Caelo	Senna leaf, cut	13136703	3
Caelo	Senna leaf, cut	1316703	2
Caelo	Senna leaf, cut	15101303	1
Caelo	Senna leaf, cut	111113a	1
Caelo	Senna leaf, cut	21011401	1
Caelo	Senna leaf, cut	12369903	1
Caelo	Senna leaf, cut	14183805	2
Caelo	Senna leaf, cut	14306310	1
Caelo	Senna leaf, cut	14306311	2
Caelo	Senna leaf, cut	14306324	1
Caelo	Senna leaf, cut	12273106	3
Caelo	Senna leaf, cut	12273115	11
Caelo	Senna leaf, cut	10126502	1
Caelo	Senna leaf, cut	12273111	10
Caelo	Senna leaf, cut	12273118	3
Caelo	Senna leaf, cut	3813E1514	1
Caelo	Senna leaf, cut	4113Q1514	1
Caelo	Senna leaf, cut	5013U01514	1
Caelo	Senna leaf, cut	131316701	1
Caelo	Senna leaf, cut	2331B120521	4
Caelo	Senna leaf, cut	514R1514	1
Caelo	Senna leaf, cut	12273104	2
Caelo	Senna leaf, cut	12115503	6
Caelo	Senna leaf, cut	12273113	3
Caelo	Senna leaf, cut	12273119	4
Caelo	Senna leaf, cut	13136704	13
Caelo	Senna leaf, cut	13136705-3489312103	1
Caelo	Senna leaf, cut	13136706	1
Caelo	Senna leaf, cut	1316706	1
Caesar & Loretz GmbH,...	Senna leaf, cut	11277303	3
Caesar & Loretz GmbH,...	Senna leaf, cut	11277308	3
Caesar & Loretz GmbH,...	Senna leaf, cut	11277314	5
Caesar & Loretz GmbH,...	Senna leaf, cut	12273103	11
Caesar & Loretz GmbH,...	Senna leaf, cut	13136708	7
Caesar&Loretz GmbH D-...	Senna leaf, cut	12115504	4
Cealo	Senna leaf, cut	12273116	15
Fagron	Senna leaf, cut	314Q1514	1
Galke	Senna leaf, cut	21778	1
Caelo	Senna leaf, cut	13136705	3
Klenk	Senna leaf, cut	2331A100525	2
Klenk	Senna leaf, cut	2331B120403	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Klenk	Senna leaf, cut	2331B150903	1
Klenk	Senna leaf, cut	2331B110907	2
Klenk	Senna leaf, cut	2331C120614	8
Klenk	Senna leaf, cut	2331B130214	5
Klenk	Senna leaf, cut	B130214	1
Klenk	Senna leaf, cut	2331C130326	16
Klenk	Senna leaf, cut	2331c130326	1
Klenk	Senna leaf, cut	2331A110207	1
Caelo	Senna leaf, cut	13136718	1
Caelo	Senna leaf, cut	13136724	1
Phönix 10.01.2014	Senna leaf, cut	13136707	1
Caelo	Senna leaf, cut	12273120	3
Sanacorp	Senna leaf, cut	13136701	6
Caelo	Senna leaf, cut	11277307	1
Caelo	Senna leaf, cut	11277301	1
Caelo	Senna leaf, cut	12115501	5
Caelo	Senna leaf, cut	12273101	4
Caelo	Senna leaf, powdered	11193307	1
Caelo	Senna leaf, powdered	15363922	1
Caelo	Senna leaf, powdered	17223202	1
Caelo	Senna leaf, powdered	14347606	1
Klenk	Senna leaf, powdered	2331B150903	1
Caelo	Senna pods, tinnevelly	11003004	1
Caelo	Senna pods, tinnevelly	11003009	2
Caelo	Senna pods, tinnevelly	22061202	1
Caelo	Senna pods, tinnevelly	110030009	1
Caelo	Senna pods, tinnevelly	12267604	1
Caelo	Senna pods, tinnevelly	12267609	3
Caelo	Senna pods, tinnevelly	11003013	1
Caelo	Senna pods, tinnevelly	122676707	1
Caelo	Senna pods, tinnevelly	12267606	1
Caelo	Senna pods, tinnevelly	12267602	2
Caelo	Senna pods, tinnevelly	12267610	1
Caelo	Senna pods, tinnevelly	12267608	1
Caelo	Senna pods, tinnevelly	12267007	1
Caelo	Senna pods, tinnevelly	12267201	1
Caelo	Senna pods, tinnevelly	12267605	1
Caesar & Loretz GmbH,...	Senna pods, tinnevelly	11003012	1
Caesar & Loretz GmbH,...	Senna pods, tinnevelly	11003014	1
Caesar & Loretz GmbH,...	Senna pods, tinnevelly	12267601	2
Caesar & Loretz GmbH,...	Senna pods, tinnevelly	12267603	1
Klenk	Senna pods, tinnevelly	1041B120327	2
Alfred Galke	Shepherd's purse, cut	20591	1
Bahnhof-Apotheke	Shepherd's purse, cut	4-120924	1
Bombastus	Shepherd's purse, cut	269594	4
Bombastus	Shepherd's purse, cut	278856	2
Bombastus	Shepherd's purse, cut	269977	1
Bombastus	Shepherd's purse, cut	284136	1
Bombastus	Shepherd's purse, cut	12345	2
Caelo	Shepherd's purse, cut	11036406	5
Caelo	Shepherd's purse, cut	14061201	1
Caelo	Shepherd's purse, cut	11091202	1
Caelo	Shepherd's purse, cut	15101202	1
Caelo	Shepherd's purse, cut	1132820111-14	1
Caelo	Shepherd's purse, cut	11328203	5
Caelo	Shepherd's purse, cut	11328204	3
Caelo	Shepherd's purse, cut	269595	1
Caelo	Shepherd's purse, cut	12354201	11
Caelo	Shepherd's purse, cut	11328209	6
Caelo	Shepherd's purse, cut	11328205	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Shepherd's purse, cut	10061301	1
Caelo	Shepherd's purse, cut	12354202	2
Caelo	Shepherd's purse, cut	12354204	16
Caelo	Shepherd's purse, cut	12354203	13
Caelo	Shepherd's purse, cut	12354001	1
Caelo	Shepherd's purse, cut	3121301	1
Caelo	Shepherd's purse, cut	12354207	2
Caelo	Shepherd's purse, cut	12354209	1
Caelo	Shepherd's purse, cut	12354206	5
Caelo	Shepherd's purse, cut	11036401	1
Caelo	Shepherd's purse, cut	12354503	1
Caelo	Shepherd's purse, cut	11328201	6
Caelo	Shepherd's purse, cut	11328208	6
Caelo	Shepherd's purse, cut	12354203-3396310111	1
Caelo	Shepherd's purse, cut	11328207	8
Caelo	Shepherd's purse, cut	11328206	2
Caelo	Shepherd's purse, cut	12254202	1
Caelo	Shepherd's purse, cut	12354205	6
Caelo	Shepherd's purse, cut	11036404	1
Galke	Shepherd's purse, cut	21719	2
Galke	Shepherd's purse, cut	19483	1
Klenk	Shepherd's purse, cut	3671A-100414	2
Klenk	Shepherd's purse, cut	3671B111201	1
Klenk	Shepherd's purse, cut	B111201	1
Caelo	Shepherd's purse, cut	13344203	1
Caelo	Shepherd's purse, cut	11036410	2
Wolf	Shepherd's purse, cut	B449	2
-	Silverweed, cut	711M-01619	1
-	Silverweed, cut	130849	1
Caelo	Silverweed, cut	20081202	1
Caelo	Silverweed, cut	8111204	1
Caelo	Silverweed, cut	11016407	1
Caelo	Silverweed, cut	11328109	13
Caelo	Silverweed, cut	11328110	1
Caelo	Silverweed, cut	11328105	7
Caelo	Silverweed, cut	11328112	2
Caelo	Silverweed, cut	11016404	1
Galke	Silverweed, cut	12891	2
Gehe	Silverweed, cut	11328101	1
Klenk	Silverweed, cut	3551A110913	1
Klenk	Silverweed, cut	H-280513-3	1
Klenk	Silverweed, cut	A110913	2
Klenk	Silverweed, cut	3551A130903	1
Phönix	Silverweed, cut	11328107	7
Klenk	Silverweed, cut	11328103	4
Euro OTC	Sodium alginate	1509036-01	1
Fagron	Sodium alginate	14G22-B99	1
phönix	Sodium alginate	11509036-02	1
Sigma-Aldrich	Sodium butyrate	Lot.091M-5302V	1
Caelo	Sodium carbonate deca...	11254706	1
Caelo	Sodium carbonate deca...	11254708	1
Caelo	Sodium carbonate deca...	12239810	2
Caelo	Sodium carbonate deca...	80136179	1
Caelo	Sodium carbonate deca...	13036907	1
Caelo	Sodium carbonate deca...	13036909	1
Caelo	Sodium carbonate deca...	13036910	1
Caelo	Sodium carbonate deca...	13036902	2
Caelo	Sodium carbonate deca...	12239806	1
Caelo	Sodium carbonate deca...	80136428	1
Phönix	Sodium carbonate deca...	13036904	2

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sodium dihydrogen pho...	12198510	2
Caelo	Sodium dihydrogen pho...	12198517	2
Caelo	Sodium dihydrogen pho...	12198506	1
Caelo	Sodium dihydrogen pho...	13D08-N25	1
Euro OTC	Sodium dihydrogen pho...	1305028-01	2
Euro OTC	Sodium dihydrogen pho...	1209004-01	2
Fagron	Sodium dihydrogen pho...	12L05-N05	1
Alliance	Sodium hydrocarbonate	12324704	1
Fagron	Sodium hydrocarbonate	12G11-N03	7
Anzag/ Hedinger	Sodium hydrocarbonate	206027	1
Caelo	Sodium hydrocarbonate	11304813	1
Caelo	Sodium hydrocarbonate	8101203	1
Caelo	Sodium hydrocarbonate	12132204	7
Caelo	Sodium hydrocarbonate	12132219	8
Caelo	Sodium hydrocarbonate	1203030-1	1
Caelo	Sodium hydrocarbonate	12356303	3
Caelo	Sodium hydrocarbonate	12324725	1
Caelo	Sodium hydrocarbonate	12324708	1
Caelo	Sodium hydrocarbonate	12356401	4
Caelo	Sodium hydrocarbonate	13060117	1
Caelo	Sodium hydrocarbonate	13186704	1
Caelo	Sodium hydrocarbonate	12356403	1
Caelo	Sodium hydrocarbonate	12356407	2
Caelo	Sodium hydrocarbonate	13234004	2
Caelo	Sodium hydrocarbonate	6011404	1
Caelo	Sodium hydrocarbonate	13234005	4
Caelo	Sodium hydrocarbonate	13234007	4
Caelo	Sodium hydrocarbonate	13234202	3
Caelo	Sodium hydrocarbonate	13390520	1
Caelo	Sodium hydrocarbonate	13234205	1
Caelo	Sodium hydrocarbonate	12132503	1
Caelo	Sodium hydrocarbonate	15328602	1
Caelo	Sodium hydrocarbonate	13101706	1
Caelo	Sodium hydrocarbonate	11304802	2
Caelo	Sodium hydrocarbonate	13186706	2
Caelo	Sodium hydrocarbonate	1234702	2
Caelo	Sodium hydrocarbonate	12109204	3
Caelo	Sodium hydrocarbonate	13060103	8
Caelo	Sodium hydrocarbonate	3012Q-01892	1
Caelo	Sodium hydrocarbonate	13060120	5
Caelo	Sodium hydrocarbonate	13390505	1
Caelo	Sodium hydrocarbonate	13186721	1
Caelo	Sodium hydrocarbonate	11304809	1
Caelo	Sodium hydrocarbonate	12132203	3
Caelo	Sodium hydrocarbonate	1219204	1
Caesar & Loretz GmbH,...	Sodium hydrocarbonate	13060102	1
Eu Rho	Sodium hydrocarbonate	1203030-01	8
Euro OCT	Sodium hydrocarbonate	1307017-01	1
Euro OTC	Sodium hydrocarbonate	120303001	1
Euro OTC	Sodium hydrocarbonate	120800801	1
Euro OTC	Sodium hydrocarbonate	1012011-01	1
Euro OTC	Sodium hydrocarbonate	1109029-01	8
Euro OTC	Sodium hydrocarbonate	1012011	1
Euro OTC	Sodium hydrocarbonate	1208008-01	9
Euro OTC	Sodium hydrocarbonate	1304017-02	2
euroho/gehe	Sodium hydrocarbonate	123030-02	1
Euro OTC	Sodium hydrocarbonate	1104013-01	2
Euro OTC	Sodium hydrocarbonate	1304017-01	5
Fagron	Sodium hydrocarbonate	11K25-N05	3
Fagron	Sodium hydrocarbonate	12D11-No2	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Sodium hydrocarbonate	13D29-N09	4
Fagron	Sodium hydrocarbonate	11/12-N16	1
Fagron	Sodium hydrocarbonate	11I12-N16	3
Fagron	Sodium hydrocarbonate	12D11-N02	9
Fagron	Sodium hydrocarbonate	13G11-N03	2
Fagron	Sodium hydrocarbonate	RBA3421100	3
Fagron	Sodium hydrocarbonate	RBA3651200	1
Fagron	Sodium hydrocarbonate	4413I01892	1
Finze	Sodium hydrocarbonate	Pr.Nr.4311Q-01892	1
fischer	Sodium hydrocarbonate	6522101	6
Fischer/VDL	Sodium hydrocarbonate	6521111	5
Gehe	Sodium hydrocarbonate	11078315	1
Gehe	Sodium hydrocarbonate	1203030-02	8
Gehe	Sodium hydrocarbonate	12k09-N05	1
Caelo	Sodium hydrocarbonate	13186711	1
Phönix	Sodium hydrocarbonate	13186705	4
Phönix	Sodium hydrocarbonate	13390515	1
Caelo	Sodium hydrocarbonate	12324702	7
Caelo	Sodium hydrocarbonate	12109205	6
Fagron	Sodium hydrocarbonate	13B18-N03	6
Caelo	Sodium hydroxide pell. ...	15312102	1
Caelo	Sodium hydroxide pell. ...	11070821	1
Fagron	Sodium hydroxide pell. ...	12E02-N15	1
Fagron	Sodium hydroxide pell. ...	13F06-N02	3
Fagron	Sodium hydroxide pell. ...	13k22-no5	1
Caelo	Sodium hydroxide pell. ...	12368105	1
Alliance healthcare	Sodium monohydrogenph. ...	12L05-N04	2
Bombastus	Sodium monohydrogenph. ...	11H04-N06	1
Fagron	Sodium monohydrogenph. ...	613I-01914	1
Fagron	Sodium monohydrogenph. ...	13D24-N12	2
Fagron	Sodium monohydrogenph. ...	13H01-B01	1
AHD	Sodium monohydrogenph. ...	112345013	1
Alliance	Sodium monohydrogenph. ...	12256606	1
Caelo	Sodium monohydrogenph. ...	1169315	1
Caelo	Sodium monohydrogenph. ...	9302613	2
Caelo	Sodium monohydrogenph. ...	11169315	1
Caelo	Sodium monohydrogenph. ...	12345001	2
Caelo	Sodium monohydrogenph. ...	12345004	7
Caelo	Sodium monohydrogenph. ...	12345007	3
Caelo	Sodium monohydrogenph. ...	12345013	6
Caelo	Sodium monohydrogenph. ...	71199028	1
Caelo	Sodium monohydrogenph. ...	12345016	7
Caelo	Sodium monohydrogenph. ...	83002059	1
Caelo	Sodium monohydrogenph. ...	12256602	2
Caelo	Sodium monohydrogenph. ...	11169309	3
Caelo	Sodium monohydrogenph. ...	11169303	2
Caelo	Sodium monohydrogenph. ...	12345025	1
Caelo	Sodium monohydrogenph. ...	AKD7	1
Caesar&lorenz,Anzag	Sodium monohydrogenph. ...	12256606	3
Fagron	Sodium monohydrogenph. ...	11K30-N01	1
Fagron	Sodium monohydrogenph. ...	2111E-01914	1
Fagron	Sodium monohydrogenph. ...	1513I-01914	1
Fagron	Sodium monohydrogenph. ...	B44888A	1
gebepfarm	Sodium monohydrogenph. ...	20160909-2	1
ICHTHYOL-GESELLSCHAFT	Sodium monohydrogenph. ...	Caelo	1
Caelo	Sodium monohydrogenph. ...	12109002	2
Caelo	Sodium monohydrogenph. ...	12109106	1
Caelo	Sodium monohydrogenph. ...	10135304	1
Caelo	Sodium monohydrogenph. ...	12109109	1
Caelo	Sodium monohydrogenph. ...	13028103	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sodium monohydrogenph...	11109513	1
Caelo	Sodium monohydrogenph...	12109108	2
Caelo	Sodium monohydrogenph...	13028001	1
Caelo	Sodium monohydrogenph...	72006059	1
Gehe	Sodium monohydrogenph...	12109001	2
Jenne	Sodium monohydrogenph...	12109003	3
Phönix	Sodium monohydrogenph...	1302800,	1
Phönix	Sodium monohydrogenph...	13028101	1
Caelo	Sodium monohydrogenph...	13028003	1
Caelo	Sodium perborate, hyd...	13050801	2
Caelo	Sodium perborate, hyd...	13050807	1
Caelo	Sodium perborate, hyd...	13050805	1
Aldrich	Sodium propionate	U02796-056	1
Sigma-Aldrich	Sodium propionate	SLBK5249V	1
Caaelo	Sodium sulfate decahy...	11294603	2
Caelo	Sodium sulfate decahy...	18101202	1
Caelo	Sodium sulfate decahy...	12157001	1
Caelo	Sodium sulfate decahy...	11012207	1
Caelo	Sodium sulfate decahy...	12256902	1
Caelo	Sodium sulfate decahy...	70706387	1
Caelo	Sodium sulfate decahy...	12157011	1
Caelo	Sodium sulfate decahy...	12157007	1
Caelo	Sodium sulfate decahy...	12157006	3
Caelo	Sodium sulfate decahy...	12157013	1
Caelo	Sodium sulfate decahy...	205026	1
Caelo	Sodium sulfate decahy...	12157012	18
Caelo	Sodium sulfate decahy...	61599506	1
EuRho	Sodium sulfate decahy...	1210005-01	2
Euro OTC	Sodium sulfate decahy...	121000502	2
Euro OTC	Sodium sulfate decahy...	1108035-01	3
Euro OTC	Sodium sulfate decahy...	1108035-02	2
Euro OTC	Sodium sulfate decahy...	1210005-02	2
Euro OTC	Sodium sulfate decahy...	4312I-01920	1
Fagron	Sodium sulfate decahy...	1464	1
Fagron	Sodium sulfate decahy...	2134	1
fargon/Sanacorp	Sodium sulfate decahy...	12H31-N04	1
Gehe	Sodium sulfate decahy...	12257902	6
Caelo	Sodium sulfate decahy...	12157005	13
Hedinger/Phönix	Sodium sulfate decahy...	205025	1
nachprüfung	Sodium sulfate decahy...	C1069	1
Unisan	Sodium sulfate decahy...	11294605	1
Caelo	Sodium sulfate decahy...	11012210	2
Caelo	Sodium sulfate decahy...	12257901	1
Caelo	Sodium thiosulfate pe...	80426288	1
Caelo	Sodium thiosulfate pe...	26041302	1
Fagron	Sodium thiosulfate pe...	13092013E	1
Fagron	Sodium thiosulfate pe...	12F20-N20	1
Fagron	Sodium thiosulfate pe...	12F20-N10	1
Fagron	Sodium thiosulfate pe...	3313U-01922	1
Caelo	Solanum dulcamara ste...	10375605	1
Caelo	Solanum dulcamara ste...	132564301	1
Caelo	Solanum dulcamara ste...	13254301	1
Caelo	Solanum dulcamara ste...	103745604	1
Klenk	Solanum dulcamara ste...	5601A080513	3
Caelo	Sorrel herb, cut	130546	1
Gahlke	Sorrel herb, cut	21479	1
Caelo	Sorrel herb, cut	13289502	2
Kräuter-Schulte	Sorrel herb, cut	55272	1
Caelo	Sour cherry stems, cut	10367019	1
Caelo	Sour cherry stems, cut	12042301	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sour cherry stems, cut	10367014	1
Caelo	Sour cherry stems, cut	12042307	1
Caelo	Spearmint leaf, cut	12133901	3
Caelo	Spearmint leaf, cut	1512Q-01505	1
Caelo	Spearmint leaf, cut	11037409+110374	1
Caelo	Spearmint leaf, cut	12133906	2
Caelo	Spearmint leaf, cut	13105001	10
Caelo	Spearmint leaf, cut	12376706	1
Caelo	Spearmint leaf, cut	12133909	1
Caelo	Spearmint leaf, cut	13105003	1
Anzag 12.03.13 ek: 4,...	St. John's wort, cut	11185608	2
Caelo	St. John's wort, cut	12092201	1
Aurica	St. John's wort, cut	521200778	1
Aurica	St. John's wort, cut	521202559	1
Bahnhof-Apotheke	St. John's wort, cut	4-121018	1
Bombastus	St. John's wort, cut	268913	1
Bombastus	St. John's wort, cut	275106	6
Bombastus	St. John's wort, cut	265761	1
Bombastus	St. John's wort, cut	268834	2
Caelo	St. John's wort, cut	4021B110321	1
Caelo	St. John's wort, cut	11185602	1
Caelo	St. John's wort, cut	11185608	18
Caelo	St. John's wort, cut	5021301	1
Caelo	St. John's wort, cut	1185608	1
Caelo	St. John's wort, cut	16041301	1
Caelo	St. John's wort, cut	12092204	1
Caelo	St. John's wort, cut	13091303	1
Caelo	St. John's wort, cut	111185608	1
Caelo	St. John's wort, cut	11185607	1
Caelo	St. John's wort, cut	30011401	1
Caelo	St. John's wort, cut	132203204	1
Caelo	St. John's wort, cut	15068105	1
Caelo	St. John's wort, cut	268913	1
Caelo	St. John's wort, cut	13203204	6
Caelo	St. John's wort, cut	13203205	1
Finze	St. John's wort, cut	9297303	1
Galke	St. John's wort, cut	21034	1
Galke	St. John's wort, cut	21990	4
Galke	St. John's wort, cut	23054	1
Galke	St. John's wort, cut	21556	1
Gehe	St. John's wort, cut	9297305	1
Gehe	St. John's wort, cut	11185602	1
Bombastus	St. John's wort, cut	281530	1
Hepart AG	St. John's wort, cut	B-445, kbA	1
Klenk	St. John's wort, cut	15068103	2
Klenk	St. John's wort, cut	4021A100819	1
Klenk	St. John's wort, cut	4021A100819	21
Klenk	St. John's wort, cut	4021A100819914	2
Klenk	St. John's wort, cut	4021A100919	1
Klenk	St. John's wort, cut	4021A-100819	1
Klenk	St. John's wort, cut	A121120	1
Klenk	St. John's wort, cut	4012A100819	1
Klenk	St. John's wort, cut	A130612	3
Klenk	St. John's wort, cut	4021A130612	4
Klenk	St. John's wort, cut	4021a100819	1
Klenk	St. John's wort, cut	4021a120604	1
Klenk	St. John's wort, cut	4021B110321	2
Klenk	St. John's wort, cut	4021A120604	16
Klenk	St. John's wort, cut	4021A120905	9
Noweda	St. John's wort, cut	12092202	6

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	St. John's wort, cut	12092209	2
Klenk	St. John's wort, cut	4021A00819	1
Wolf	St. John's wort, cut	206152	1
Wolf	St. John's wort, cut	B206152	1
Wolf	St. John's wort, cut	19468	2
Wolf	St. John's wort, cut	B-455	2
Wolf	St. John's wort, cut	B-424	1
Caelo	Star anise	10169101	1
Caelo	Star anise	10376403	2
Caelo	Star anise	11314104	1
Caelo	Star anise	12226211	1
Caelo	Star anise	10376405	1
Caelo	Star anise	11314103	1
Klenk	Star anise	2690A101026	1
Klenk	Star anise	2690A111013	3
Klenk	Star anise	2696B111109	1
Klenk	Star anise	B111109	1
Klenk	Star anise	2690A120809	1
Klenk	Star anise	2690A130903	2
Caelo	Star anise, cut	16253201	2
Caelo	Stemless carline root	23071203	1
Caelo	Stemless carline root	12144804	1
Caelo	Stemless carline root	13130303	1
Caelo	Stemless carline root	13033501	1
Caelo	Stemless carline root	25111306	1
Caelo	Stemless carline root	14347401	1
Caelo	Stemless carline root	13130301	6
Caelo	Stemless carline root	13130304	1
Caelo	Stemless carline root	12232803	1
Hepart AG	Stemless carline root	B120726	1
Klenk	Stemless carline root	12097301	1
Klenk	Stemless carline root	B110831	1
Klenk	Stemless carline root	6194b110831	1
Klenk	Stemless carline root	6194B110831	1
Klenk	Stemless carline root	6191B120726	3
Klenk	Stemless carline root	69191B120726	1
Nachprüfung	Stemless carline root	2812U02133	1
Noweda	Stemless carline root	12163702	1
Caelo	Strawberry leaf, cut	11117909	1
Caelo	Strawberry leaf, cut	5122013c	1
Klenk	Strawberry leaf, cut	2031B110224	2
Klenk	Strawberry leaf, cut	B120925	1
Klenk	Strawberry leaf, cut	A130430	1
Klenk	Strawberry leaf, cut	2031A130430	2
Caelo	Sulfamerazine	10218401	1
Fagron	Sulfanilamide	11L01-No8	1
Klenk	Sunflower, cut	1711I-07036	1
Klenk	Sunflower, cut	1701B091013	1
Fagron	Sweet fennel	2870A130304	3
Fargron/Noweda	Sweet fennel	2870A150810	1
Klenk	Sweet fennel	2870A140528	2
Klenk	Sweet fennel	2870130304A	1
Klenk	Sweet fennel	2870A131002	1
Anzag	Sweet woodruff herb, ...	12103504	2
Caelo	Sweet woodruff herb, ...	10375802	1
Caelo	Sweet woodruff herb, ...	4409M-01621	1
Caelo	Sweet woodruff herb, ...	52236077	1
Caelo	Sweet woodruff herb, ...	10375812	1
Caelo	Sweet woodruff herb, ...	18031304	1
Caelo	Sweet woodruff herb, ...	12103508	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Sweet woodruff herb, ...	12103510	1
Caelo	Sweet woodruff herb, ...	12103513	2
Caelo	Sweet woodruff herb, ...	12103509	1
Caelo	Sweet woodruff herb, ...	12103514	1
Gahlke	Sweet woodruff herb, ...	22100	1
Klenk	Sweet woodruff herb, ...	3601B090114	1
Klenk	Sweet woodruff herb, ...	B090114	3
Klenk	Sweet woodruff herb, ...	3601B140321	1
Kräuter-Schulte	Sweet woodruff herb, ...	52878	1
Caelo	Talcum	11318324	4
Caelo	Talcum	28121201	1
Caelo	Talcum	11164313	1
Caelo	Talcum	11164306	1
Caelo	Talcum	12267401	4
Caelo	Talcum	9218303	1
Caelo	Talcum	12267412	7
Caelo	Talcum	11318312	2
Caelo	Talcum	15061301	1
Caelo	Talcum	13146301	1
Caelo	Talcum	13146308	6
Caelo	Talcum	13146307	3
Caelo	Talcum	13146312	4
Caelo	Talcum	2011406	1
Caelo	Talcum	13146316	3
Caelo	Talcum	13146315	1
Caelo	Talcum	12267424	5
Caelo	Talcum	12267423	3
Caelo	Talcum	11318311	3
Caelo	Talcum	11318335	4
Caelo	Talcum	13146302	8
Caelo	Talcum	11318301	1
EuRho	Talcum	1105024-02	1
Euro OTC	Talcum	1205046-01	2
Euro OTC	Talcum	1305022-01	7
Euro OTC	Talcum	1210052-01	4
Euro OTC	Talcum	1305022-02	1
Phönix	Talcum	10148805Retest	1
Caelo	Tall golden rod, cut	12343103	17
Anzag 17.04.13 ek: 2,...	Tall golden rod, cut	4521A110816	2
Aurica	Tall golden rod, cut	521201267	1
Aurica	Tall golden rod, cut	224133	1
Bomba/AHD	Tall golden rod, cut	279526	1
Bombastus	Tall golden rod, cut	261756	1
Bombastus	Tall golden rod, cut	271459	1
Bombastus	Tall golden rod, cut	270047	2
Bombastus	Tall golden rod, cut	271460	1
Bombastus	Tall golden rod, cut	278697	2
Bombastus	Tall golden rod, cut	209974	1
Caelo	Tall golden rod, cut	314050-1-p	1
Caelo	Tall golden rod, cut	11207010	3
Caelo	Tall golden rod, cut	15061203	1
Caelo	Tall golden rod, cut	265283	1
Caelo	Tall golden rod, cut	11280301	4
Caelo	Tall golden rod, cut	17091203	1
Caelo	Tall golden rod, cut	11280308	9
Caelo	Tall golden rod, cut	20111209	1
Caelo	Tall golden rod, cut	112080308	1
Caelo	Tall golden rod, cut	12319002	2
Caelo	Tall golden rod, cut	28051302	1
Caelo	Tall golden rod, cut	6081302	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Tall golden rod, cut	12343104	5
Caelo	Tall golden rod, cut	4091302	1
Caelo	Tall golden rod, cut	12343102	3
Caelo	Tall golden rod, cut	14112012	1
Caelo	Tall golden rod, cut	27121302	1
Caelo	Tall golden rod, cut	4021405	1
Caelo	Tall golden rod, cut	12343109	1
Caelo	Tall golden rod, cut	13386903	1
Caelo	Tall golden rod, cut	13386901	1
Caelo	Tall golden rod, cut	14018404	1
Caelo	Tall golden rod, cut	2656153	1
Caelo	Tall golden rod, cut	12343105	1
Caelo	Tall golden rod, cut	11280309	1
Caelo	Tall golden rod, cut	12336801	1
Caelo	Tall golden rod, cut	12319007	21
Caelo	Tall golden rod, cut	12319006	3
Caelo	Tall golden rod, cut	12319004	10
Caelo	Tall golden rod, cut	4113A-01684	1
Caelo	Tall golden rod, cut	11280310	6
Caelo	Tall golden rod, cut	12343106	1
Caesar & Loretz GmbH,...	Tall golden rod, cut	11207014	3
Galke	Tall golden rod, cut	21079	2
Gehe	Tall golden rod, cut	11207011	1
Gehe	Tall golden rod, cut	11280311	2
Caelo	Tall golden rod, cut	12343101	3
Klenk	Tall golden rod, cut	A110209	1
Klenk	Tall golden rod, cut	4521A-110816	1
Klenk	Tall golden rod, cut	4521A100414	1
Klenk	Tall golden rod, cut	4521A110209	4
Noweda	Tall golden rod, cut	11280306	3
Caelo	Tall golden rod, cut	12319003	22
Bombastus	Tall golden rod, cut	274290	1
Caelo	Tall hawkweed, cut	3611b111005	1
Klenk	Tall hawkweed, cut	B111005	1
Klenk	Tall hawkweed, cut	3611B11105	1
Caelo	Tall nasturtium herb,...	12031602	1
Caelo	Tall nasturtium herb,...	12031601	1
Caelo	Tall nasturtium herb,...	12031606	1
Caelo	Tall nasturtium herb,...	12031603	1
Caelo	Tall nasturtium herb,...	12031604	2
Caelo	Tall nasturtium herb,...	13104401	4
Caelo	Tall nasturtium herb,...	107063	1
Caelo	Tall nasturtium herb,...	12031605	1
Caelo	Tall nasturtium herb,...	13104402	2
Caelo	Tall nasturtium herb,...	13104404	2
Caelo	Tall nasturtium herb,...	13104405	1
Caelo	Tall nasturtium herb,...	13104403	5
Caelo	Tall nasturtium herb,...	13104406	1
Caelo	Theriac, powdered	12289301	4
Caelo	Theriac, powdered	11082413	1
Caelo	Theriac, powdered	2021301	1
Caelo	Theriac, powdered	15101307	1
Caelo	Theriac, powdered	412091-2P	1
Caelo	Theriac, powdered	12289312	1
Caelo	Theriac, powdered	13407304	2
Caelo	Theriac, powdered	15026401	2
Caelo	Theriac, powdered	11081515	1
Caelo	Theriac, powdered	15312501	2
Caelo	Theriac, powdered	1531501	1
Caelo	Theriac, powdered	15312511	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Theriac, powdered	14156501	1
Caelo	Theriac, powdered	12289307	8
Caelo	Theriac, powdered	12189404	2
Caelo	Theriac, powdered	12289305	2
Caelo	Theriac, powdered	15312508	1
Caelo	Theriac, powdered	12289303	1
Caelo	Theriac, powdered	12289306	1
Caelo	Theriac, powdered	15312504	1
Caelo	Theriac, powdered	12189401	1
Caesar/Noweda	Theriac, powdered	12289309	1
Klenk	Theriac, powdered	12189403	1
Caelo	Thiomersal	10296413	1
Caelo	Thiomersal	21051507	1
Caesar & Loretz GmbH	Thiomersal	12275218	1
Fagron	Thiomersal	12F19-N11	1
Fagron	Thiomersal	12J17-N02	1
Fagron	Thiomersal	12J17-N02	1
Aurica	Thyme, rubbed	521207003	1
Bahnhof-Apotheke	Thyme, rubbed	17-121112	1
Bombastus	Thyme, rubbed	277996	2
Bombastus	Thyme, rubbed	277466	1
Bombastus	Thyme, rubbed	243485	1
Caelo	Thyme, rubbed	10365807	2
Caelo	Thyme, rubbed	10365816	1
Caelo	Thyme, rubbed	8061206	1
Caelo	Thyme, rubbed	11345004	4
Caelo	Thyme, rubbed	15101201	1
Caelo	Thyme, rubbed	12111201	1
Caelo	Thyme, rubbed	11345007	5
Caelo	Thyme, rubbed	21121204	1
Caelo	Thyme, rubbed	11345001	1
Caelo	Thyme, rubbed	11345010	6
Caelo	Thyme, rubbed	29011303	1
Caelo	Thyme, rubbed	11021301	1
Caelo	Thyme, rubbed	22021301	1
Caelo	Thyme, rubbed	23021304	1
Caelo	Thyme, rubbed	26021301	1
Caelo	Thyme, rubbed	4041301	1
Caelo	Thyme, rubbed	11345014	12
Caelo	Thyme, rubbed	25041302	1
Caelo	Thyme, rubbed	11345013	9
Caelo	Thyme, rubbed	1134514	1
Caelo	Thyme, rubbed	13081301	1
Caelo	Thyme, rubbed	25091304	1
Caelo	Thyme, rubbed	29101301	1
Caelo	Thyme, rubbed	11121306	1
Caelo	Thyme, rubbed	13011402	1
Caelo	Thyme, rubbed	13048308	2
Caelo	Thyme, rubbed	16011401	1
Caelo	Thyme, rubbed	4021512	1
Caelo	Thyme, rubbed	13048314	1
Caelo	Thyme, rubbed	14119001	1
Caelo	Thyme, rubbed	15104401	1
Caelo	Thyme, rubbed	11345002	1
Caelo	Thyme, rubbed	11345006	3
Caelo	Thyme, rubbed	13048302	2
Caelo	Thyme, rubbed	13048301	14
Caelo	Thyme, rubbed	13048309	4
Caelo	Thyme, rubbed	10365815	2
Caelo	Thyme, rubbed	11345011	13

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Thyme, rubbed	13048309-3475312161	1
Euro OTC	Thyme, rubbed	4622A130109	75
Galke	Thyme, rubbed	19386	2
Galke	Thyme, rubbed	28719	1
Galke	Thyme, rubbed	20719	2
Galke	Thyme, rubbed	1833	1
Gehe	Thyme, rubbed	4622A110120	1
Klenk	Thyme, rubbed	4622A110728	25
Klenk	Thyme, rubbed	4622A120111	35
Hepart AG	Thyme, rubbed	A130109	2
Klenk	Thyme, rubbed	4622a110728	1
Klenk	Thyme, rubbed	1910211688	1
Klenk	Thyme, rubbed	4622a130109	2
Klenk	Thyme, rubbed	4622A141203	1
Klenk	Thyme, rubbed	4622B110519	1
Klenk	Thyme, rubbed	2103311688	1
Klenk	Thyme, rubbed	A130910	3
Klenk	Thyme, rubbed	4622A130910	2
Klenk	Thyme, rubbed	4622A12011	1
Klenk	Thyme, rubbed	4622A-120111	1
Klenk	Thyme, rubbed	4622a120111	3
Noweda	Thyme, rubbed	521303908	1
Bombastus	Thyme, rubbed	273909	3
Caelo	Thyme, rubbed		1
Weltecke	Thyme, rubbed	67101212	1
Caelo	Tonka beans	1078C	1
Caelo	Tonka beans	12145101	2
Caelo	Tonka beans	12144101	1
Caelo	Tonka beans	20111312	1
Noweda	Tonka beans	1040A111026	1
Caelo	Tormentil	11102010	1
Caelo	Tormentil	12040704	2
Caelo	Tormentil	10081203	1
Caelo	Tormentil	2512A-02188	1
Caelo	Tormentil	12040717	1
Caelo	Tormentil	12216802	1
Caelo	Tormentil	12040707	1
Caelo	Tormentil	411082-2-P	1
Caelo	Tormentil	30011405	1
Caelo	Tormentil	25022014A	1
Caelo	Tormentil	14008005	1
Caelo	Tormentil	15085501	1
Caelo	Tormentil	14360103	1
Caelo	Tormentil	15178203	1
Caelo	Tormentil	15178206	1
Caelo	Tormentil	15364316	1
Caelo	Tormentil	14008001	2
Caelo	Tormentil	15364302	5
Caelo	Tormentil	4753268	1
Caelo	Tormentil	12040708	9
Caelo	Tormentil	12040713	1
Caelo	Tormentil	1914A-02188	1
Caelo	Tormentil	14140001	1
Caelo	Tormentil	15178202	2
Caelo	Tormentil	12216803	4
Caelo	Tormentil	12216805	1
Caelo	Tormentil	14008002	2
Caelo	Tormentil	12216801	4
Cealo/Gehe	Tormentil	14140006	3
Galke	Tormentil	21091	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Galke	Tormentil	21744	2
Caelo	Tormentil	13220502	1
Klenk	Tormentil	6911B131029	4
Klenk	Tormentil	6911B141114	2
Klenk	Tormentil	6911B150825	4
Klenk	Tormentil	6911B140227	1
Klenk	Tormentil	6911B111013	10
Klenk	Tormentil	6914b120112	1
kräuter schulte	Tormentil	51952	1
Noweda10.02.2017	Tormentil	15364313	1
phönix	Tormentil	15364343	1
Phönix	Tormentil	15364302	1
Richter	Tormentil	P209904	1
Sanacorp	Tormentil	12040712	3
AHD	Tragacanth, powdered	15379906	3
Caelo	Tragacanth, powdered	8081201	1
Caelo	Tragacanth, powdered	9081202	1
Caelo	Tragacanth, powdered	15121203	1
Caelo	Tragacanth, powdered	11128905	1
Caelo	Tragacanth, powdered	12285402	1
Caelo	Tragacanth, powdered	14011302	1
Caelo	Tragacanth, powdered	12285403	4
Caelo	Tragacanth, powdered	1228503	1
Caelo	Tragacanth, powdered	15041302	1
Caelo	Tragacanth, powdered	13095203	1
Caelo	Tragacanth, powdered	13095208	3
Caelo	Tragacanth, powdered	20111305	1
Caelo	Tragacanth, powdered	7021402	1
Caelo	Tragacanth, powdered	13277802	4
Caelo	Tragacanth, powdered	14162205	7
Caelo	Tragacanth, powdered	15085607	1
Caelo	Tragacanth, powdered	153799	1
Caelo	Tragacanth, powdered	16110802	2
Caelo	Tragacanth, powdered	14162207	1
Caelo	Tragacanth, powdered	13204701	4
Caelo	Tragacanth, powdered	15085606	6
Caelo	Tragacanth, powdered	13277804	3
Caelo	Tragacanth, powdered	15085602	1
Caelo	Tragacanth, powdered	12108806	1
Caelo	Tragacanth, powdered	1327802	1
Caelo	Tragacanth, powdered	12285408	1
Caelo	Tragacanth, powdered	16110807	2
Caelo	Tragacanth, powdered	16350004	1
Fagron	Tragacanth, powdered	13204705	5
JENNE	Tragacanth, powdered	16110801	1
Noweda	Tragacanth, powdered	14162207	1
Caelo	Tragacanth, powdered	15085602	4
Fagron	Triamcinolone acetoni...	12107-N04	1
Fagron	Triamcinolone acetoni...	11g14-n02	1
Fagron	Triamcinolone acetoni...	11G14-N02	1
Fagron	Triamcinolone acetoni...	13F21-N01	2
Fagron	Triamcinolone acetoni...	12F21-N01	1
Fagron	Triamcinolone acetoni...	14F17-N02	1
Fagron	Triamcinolone acetoni...	13A15-N05	1
Fagron	Triamcinolone acetoni...	13F20-N010113/150	1
Fagron	Triamcinolone acetoni...	12107-N04022/359	1
Fagron	Triamcinolone acetoni...	12I07-No4	1
Fagron	Triamcinolone acetoni...	12G23-N06	2
Fagron	Triamcinolone acetoni...	12I07-N04	1
Fargon/17.07.2013/Now...	Triamcinolone acetoni...	12I07-N04	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Fagron	Triamcinolone acetoni...	12A05-N07	3
Fagron	Triamcinolone acetoni...	12E23-N01	2
Caelo	Tricalcium phosphate	1056303	1
EuRho	Tricalcium phosphate	13031203	1
Euro OTC	Tricalcium phosphate	1206002-01	3
Euro OTC	Tricalcium phosphate	1304025-01	2
Fagron	Tricalcium phosphate	12I13-N03	1
Anzag	Trichloroacetic acid	12135204	2
Apomix	Trichloroacetic acid	12G04-M11	1
Caelo	Trichloroacetic acid	12135201	1
Caelo	Trichloroacetic acid	12g04m11	1
Caelo	Trichloroacetic acid	11294318	1
Caelo	Trichloroacetic acid	12135203	1
Caelo	Trichloroacetic acid	12135210	2
Caelo	Trichloroacetic acid	6091306	1
Caelo	Trichloroacetic acid	14101711	1
Caelo	Trichloroacetic acid	13056203	3
Caelo	Trichloroacetic acid	12135207	5
Caelo	Trichloroacetic acid	13056212	1
Caelo	Trichloroacetic acid	10379401	1
Caelo	Trichloroacetic acid	10130802	1
Fagron	Trichloroacetic acid	13B19-M04	1
Fagron	Trichloroacetic acid	13H22-M04	1
Merck	Trichloroacetic acid	12821	1
Caelo	Trichloroacetic acid	13056213	1
Caelo	Trichloroacetic acid	13056209	1
Caelo	Turmeric root, cut	12136504	1
Caelo	Turmeric root, cut	12136506	1
Caelo	Turmeric root, cut	12136507	1
Caelo	Turmeric root, cut	1213650	1
Caelo	Turmeric root, cut	13360204	2
Caelo	Turmeric root, cut	15158001	2
Caelo	Turmeric root, cut	15158001	2
Caelo	Turmeric root, cut	15372603	1
Caelo	Turmeric root, cut	16344604	2
Caelo	Turmeric root, cut	15207601	1
Caelo	Turmeric root, cut	12136501	2
Caelo	Turmeric root, cut	12136503	2
Galke	Turmeric root, cut	20184	1
Galke	Turmeric root, cut	23123	1
Klenk	Turmeric root, cut	6741B121030	1
Bombastus	Turmeric, javanese, cut	288629	1
Bombastus	Turmeric, javanese, cut	262792	1
Bombastus	Turmeric, javanese, cut	277130	1
Bombastus	Turmeric, javanese, cut	282221	2
Bombastus	Turmeric, javanese, cut	28221	1
Bombastus	Turmeric, javanese, cut	284242	2
Caelo	Turmeric, javanese, cut	25041313	1
Caelo	Turmeric, javanese, cut	12319201	1
Caelo	Turmeric, javanese, cut	13262907	1
Caelo	Turmeric, javanese, cut	14309503	1
Caelo	Turmeric, javanese, cut	15120202	2
Caelo	Turmeric, javanese, cut	16094101	1
Caelo	Turmeric, javanese, cut	14017706	1
Caelo	Turmeric, javanese, cut	11182903	1
Caelo	Turmeric, javanese, cut	17042002	1
Caelo	Turmeric, javanese, cut	12319206	2
Caelo	Turmeric, javanese, cut	17042003	1
Caelo	Turmeric, javanese, cut	12319206	2
Galke	Turmeric, javanese, cut	15540	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Galke	Turmeric, javanese, cut	15540	1
Kenk / Phoenix	Turmeric, javanese, cut	6731B130117	1
Klenk	Turmeric, javanese, cut	B130117	1
Klenk	Turmeric, javanese, cut	6731B150630	1
Noweda	Turmeric, javanese, cut	6731B180412	1
Klenk	Valerian root, cut	6641B120417	1
Aurica	Valerian root, cut	221838	2
Bombastus	Valerian root, cut	267863	1
Bombastus	Valerian root, cut	274722	1
Bombastus	Valerian root, cut	269457	1
Caelo	Valerian root, cut	12033812	8
Caelo	Valerian root, cut	11103601	1
Caelo	Valerian root, cut	11103602	1
Caelo	Valerian root, cut	11103608	1
Caelo	Valerian root, cut	11349101	4
Caelo	Valerian root, cut	11103612	2
Caelo	Valerian root, cut	3091202	1
Caelo	Valerian root, cut	11035002	1
Caelo	Valerian root, cut	31101202	1
Caelo	Valerian root, cut	11103607	3
Caelo	Valerian root, cut	31121201	1
Caelo	Valerian root, cut	12033805	4
Caelo	Valerian root, cut	2712A-02167	1
Caelo	Valerian root, cut	12033809	9
Caelo	Valerian root, cut	1203381	1
Caelo	Valerian root, cut	20081303	1
Caelo	Valerian root, cut	12033810	1
Caelo	Valerian root, cut	120338012	1
Caelo	Valerian root, cut	28101303	1
Caelo	Valerian root, cut	29101303	1
Caelo	Valerian root, cut	13287402	3
Caelo	Valerian root, cut	15175205	1
Caelo	Valerian root, cut	12033811	5
Caelo	Valerian root, cut	11103609	4
Caelo	Valerian root, cut	12033807	1
Caelo	Valerian root, cut	13119001	1
Caelo	Valerian root, cut	13119004	3
Caelo	Valerian root, cut	13119003	12
Caelo	Valerian root, cut	13196806	6
Caelo	Valerian root, cut	13196801-3564412081	1
Caelo	Valerian root, cut	13196802	4
Galke	Valerian root, cut	22070	1
Galke	Valerian root, cut	21798	4
Klenk	Valerian root, cut	13196808	1
Klenk	Valerian root, cut	6641B110317	2
Klenk	Valerian root, cut	6641B-110317	1
Klenk	Valerian root, cut	6641B100823	1
Klenk	Valerian root, cut	6645B130226	1
Klenk	Valerian root, cut	6641B130226	9
Caelo	Valerian root, cut	13119002	18
Caelo	Valerian root, cut	1319003	1
Sanacorp	Valerian root, cut	12033804	9
Caelo	Valerian root, cut	12033808	7
Berkel AHK	Valerian root, powdered	13287406	1
Berkel AHK	Valerian root, powdered	14179403	2
Caelo	Valerian root, powdered	13287402	2
Caelo	Valerian root, powdered	15175204	1
an	Verbena herb, cut	12383007	1
Aurica	Verbena herb, cut	521305668	1
Caelo	Verbena herb, cut	11031106	5

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Verbena herb, cut	11031108	5
Caelo	Verbena herb, cut	11031103	1
Caelo	Verbena herb, cut	11031110	6
Caelo	Verbena herb, cut	19111205	1
Caelo	Verbena herb, cut	12187601	15
Caelo	Verbena herb, cut	12178601	1
Caelo	Verbena herb, cut	12188203	6
Caelo	Verbena herb, cut	4651b120611	1
Caelo	Verbena herb, cut	13151001	18
Caelo	Verbena herb, cut	12383002	2
Caelo	Verbena herb, cut	6111301	1
Caelo	Verbena herb, cut	12383005	1
Caelo	Verbena herb, cut	13351401	1
Caelo	Verbena herb, cut	15012405	1
Caelo	Verbena herb, cut	11031105	2
Caelo	Verbena herb, cut	12188202	14
Caelo	Verbena herb, cut	2x12188202	1
Caelo	Verbena herb, cut	13151003	5
Gehe	Verbena herb, cut	4651B110310	2
Klenk	Verbena herb, cut	4651A070828	3
Klenk	Verbena herb, cut	4654B120611	1
Klenk	Verbena herb, cut	A130923	1
Klenk	Verbena herb, cut	4651B130611	2
Klenk	Verbena herb, cut	4651B120611	17
Caelo	Verbena herb, cut	110031110	1
Bombastus	Walnut bark, cut	711B1206130	1
Caelo	Walnut bark, cut	11016604	1
Caelo	Walnut bark, cut	11325606	2
Caelo	Walnut bark, cut	11325605	1
Caelo	Walnut bark, cut	11016605	1
Caelo	Walnut bark, cut	11325603	1
Fiebig 16.11.12 ek:2,35	Walnut bark, cut	711B111020	5
Gehe	Walnut bark, cut	711B110128	3
Klenk	Walnut bark, cut	711B120613	3
Klenk	Walnut bark, cut	711B080806	1
Klenk	Walnut bark, cut	711b120613	1
Klenk	Walnut bark, cut	711B120906	2
ANZAG	Walnut leaf, cut	12124603	15
Anzag ek: 4,58EUR 25.09...	Walnut leaf, cut	2111A120123	9
Caelo	Walnut leaf, cut	11103010	5
ApoFit/Noweda	Walnut leaf, cut	271137	1
Caelo	Walnut leaf, cut	10050416	1
Caelo	Walnut leaf, cut	11103003	2
Caelo	Walnut leaf, cut	11103004	2
Caelo	Walnut leaf, cut	11103007	6
Caelo	Walnut leaf, cut	11103008	5
Caelo	Walnut leaf, cut	3051301	1
Caelo	Walnut leaf, cut	1214603	1
Caelo	Walnut leaf, cut	11103001	1
Caelo	Walnut leaf, cut	12124602	3
Caelo	Walnut leaf, cut	25041404	1
Caelo	Walnut leaf, cut	12124502	1
Caelo	Walnut leaf, cut	14064903	1
Caelo	Walnut leaf, cut	14064906	3
Caelo	Walnut leaf, cut	8071502	1
Caelo	Walnut leaf, cut	15126004	1
Caelo	Walnut leaf, cut	15126003	6
Caelo	Walnut leaf, cut	12124601	8
Caelo	Walnut leaf, cut	16044002	2
Caelo	Walnut leaf, cut	16044008	1

continued on the next page

continued from previous page

Supplier	Substance	Batch	Spectra
Caelo	Walnut leaf, cut	15126002	1
Caelo	Walnut leaf, cut	3712Q-01499	1
Caelo	Walnut leaf, cut	12124603-341930192	1
Caelo	Walnut leaf, cut	1414Q01499	1
Caelo	Walnut leaf, cut	14064909	2
Caelo	Walnut leaf, cut	14064910	1
Caelo	Walnut leaf, cut	14064902	4
Caelo	Walnut leaf, cut	4713U01499	1
Caelo	Walnut leaf, cut	414Q1499	1
Caelo	Walnut leaf, cut	12124605	8
Caelo	Walnut leaf, cut	14064904	4
Caelo	Walnut leaf, cut	15126008	5
Galke	Walnut leaf, cut	21061	1
Gehe	Walnut leaf, cut	10050412	1
Gehe	Walnut leaf, cut	2111B151028	2
Hepart AG	Walnut leaf, cut	A120123	1
Caelo	Walnut leaf, cut	11103009	1
Klenk	Walnut leaf, cut	2111A110816	1
Klenk	Walnut leaf, cut	F-280513-1	1
Klenk	Walnut leaf, cut	A130410	1
Klenk	Walnut leaf, cut	2111A131029	1
Klenk	Walnut leaf, cut	2111A130410	4
Klenk	Walnut leaf, cut	2111A-120123	1
Klenk	Walnut leaf, cut	211B151028	1
noweda	Walnut leaf, cut		1
Caelo	White deadnettle flower	10081206	1
Caelo	White deadnettle flower	12152402	2
Caelo	White deadnettle flower	11371610	5
Caelo	White deadnettle flower	11371609	3
Caelo	White deadnettle flower	2101301	1
Caelo	White deadnettle flower	11371613	2
Caelo	White deadnettle flower	15299101	1
Caelo	White deadnettle flower	52470437	1
Galke	White deadnettle flower	21691	4
Galke	White deadnettle flower	22704	1
Klenk	White deadnettle flower	1470A120111	4
Caelo	White deadnettle flower	11371611	2
Caelo	White deadnettle flower	12275802	1
Klenk	White deadnettle flower	1470A080103	1
Caelo	White deadnettle herb...	11371702	1
Caelo	White deadnettle herb...	11371706	3
Caelo	White deadnettle herb...	11371709	2
Caelo	White deadnettle herb...	11371711	2
Caelo	White deadnettle herb...	11371705	1
Caelo	White deadnettle herb...	11371712	1
Caelo	White deadnettle herb...	11371703	1
Galke	White deadnettle herb...	22253	2
Galke	White deadnettle herb...	19706	1
Caelo	White mustard seed	15120304	1
Caelo	White mustard seed, p...	7254a110823	1
Caelo	White mustard seed, p...	12375701	1
Caelo	White mustard seed, p...	12375705	1
Caelo	White mustard seed, p...	12375706	2
Caelo	White mustard seed, p...	12375704	1
Caelo	White mustard seed, p...	12375705	4
Caelo	White mustard seed, p...	13224804	3
Caelo	White mustard seed, p...	13224801	1
Caelo	White mustard seed, p...	12375702	1
Klenk	White mustard seed, p...	7254A141202	1
Caelo	White mustard seed, p...	11114409	1

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Supplier	Substance	Batch	Spectra
Caelo	Wild apple, sweet	11229805	1
Bombastus	Wild pansy, cut	276259	3
Bombastus	Wild pansy, cut	280890	1
Bombastus	Wild pansy, cut	274237	2
Bombastus	Wild pansy, cut	272832	1
Bombastus	Wild pansy, cut	278106	2
Bombastus	Wild pansy, cut	279314	3
Bombastus	Wild pansy, cut	282661	2
Bombastus	Wild pansy, cut	278106	2
Bombastus	Wild pansy, cut	220232	1
Caelo	Wild pansy, cut	10291007	1
Caelo	Wild pansy, cut	13091205	1
Caelo	Wild pansy, cut	10291009	3
Caelo	Wild pansy, cut	17101205	1
Caelo	Wild pansy, cut	5021304	1
Caelo	Wild pansy, cut	15021301	1
Caelo	Wild pansy, cut	11216103	2
Caelo	Wild pansy, cut	12189203	4
Caelo	Wild pansy, cut	14061311	1
Caelo	Wild pansy, cut	7101303	1
Caelo	Wild pansy, cut	12382806	1
Caelo	Wild pansy, cut	12189204	4
Caelo	Wild pansy, cut	12189204	10
Caelo	Wild pansy, cut	12189204-3458312120	1
Caelo	Wild pansy, cut	1289203	1
Caelo	Wild pansy, cut	12189203	5
Caelo	Wild pansy, cut	12382802	1
Caelo	Wild pansy, cut	12189204-3463312101	1
Fagron	Wild pansy, cut		1
Gehe	Wild pansy, cut	11216103	3
Klenk	Wild pansy, cut	4681A110303	2
Klenk	Wild pansy, cut	4681A120806	1
Klenk	Wild pansy, cut	B130715	1
Klenk	Wild pansy, cut	4681B130715	5
Klenk	Wild pansy, cut	4681A-120806	1
Klenk	Wild pansy, cut	4681A120806	15
Nachprüfung	Wild pansy, cut	10291007	1
Sanacorp	Wild pansy, cut	12221-01694	1
-	Wild thyme, cut	131023	1
-	Wild thyme, cut	130685	1
Caelo	Wild thyme, cut	11031203	1
Caelo	Wild thyme, cut	11374805	5
Caelo	Wild thyme, cut	11374805i.O.	1
Caelo	Wild thyme, cut	4501A120813	2
Caelo	Wild thyme, cut	13086805	3
Caelo	Wild thyme, cut	11374803	1
Caesar & Loretz GmbH,...	Wild thyme, cut	11374802	1
Finze	Wild thyme, cut	11031204	1
Gehe	Wild thyme, cut	1090413	1
vedono	Wild thyme, cut	11374807	2
Bomba/AHD	Willow bark, cut	280362	1
Bombastus	Willow bark, cut	261615	1
Bombastus	Willow bark, cut	277005	3
Bombastus	Willow bark, cut	278458	2
Bombastus	Willow bark, cut	277847	1
Bombastus	Willow bark, cut	288869	1
Bombastus	Willow bark, cut	251385	1
Bombastus	Willow bark, cut	292710	1
Bombastus	Willow bark, cut	282270	1
Bombastus	Willow bark, cut	281533	2

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Supplier	Substance	Batch	Spectra
Bombastus	Willow bark, cut	161594	1
Caelo	Willow bark, cut	11073210	3
Caelo	Willow bark, cut	11073201	1
Caelo	Willow bark, cut	12185201	5
Caelo	Willow bark, cut	21011302	1
Caelo	Willow bark, cut	12185206	5
Caelo	Willow bark, cut	11073208	1
Caelo	Willow bark, cut	2185206	1
Caelo	Willow bark, cut	12185208	12
Caelo	Willow bark, cut	9071301	1
Caelo	Willow bark, cut	13180702	4
Caelo	Willow bark, cut	13180705	1
Caelo	Willow bark, cut	12185204	4
Caelo	Willow bark, cut	12185207	3
Caelo	Willow bark, cut	13180701	1
Caelo	Willow bark, cut	13180705-3530411072	1
Galke	Willow bark, cut	20338	1
Klenk	Willow bark, cut	811B100910	3
Klenk	Willow bark, cut	B100910	6
Noweda	Willow bark, cut	4609A-01305	1
Caelo	Willow herb, cut	11347318	2
Caelo	Willow herb, cut	11347311	1
Caelo	Willow herb, cut	13104702	1
Caelo	Willow herb, cut	11347316	1
Caelo	Willow herb, cut	13200203	1
Caelo	Willowherb, small flo...	12064506	1
Bahnhof-Apotheke	Willowherb, small flo...	17-121107	1
Bombastus	Willowherb, small flo...	281846	2
Caelo	Willowherb, small flo...	7071201	1
Caelo	Willowherb, small flo...	9378908	1
Caelo	Willowherb, small flo...	29121201	1
Caelo	Willowherb, small flo...	2412E-01641	1
Caelo	Willowherb, small flo...	1031301	1
Caelo	Willowherb, small flo...	18031305	1
Caelo	Willowherb, small flo...	28031318	1
Caelo	Willowherb, small flo...	12041301	1
Caelo	Willowherb, small flo...	21061307	1
Caelo	Willowherb, small flo...	13071301	1
Caelo	Willowherb, small flo...	10326107	1
Caelo	Willowherb, small flo...	2081305	1
Caelo	Willowherb, small flo...	412041	1
Caelo	Willowherb, small flo...	16081302	1
Caelo	Willowherb, small flo...	16081304	1
Caelo	Willowherb, small flo...	15101302	1
Caelo	Willowherb, small flo...	13200203	7
Caelo	Willowherb, small flo...	31101303	1
Caelo	Willowherb, small flo...	15011411	1
Caelo	Willowherb, small flo...	13355906	2
Caelo	Willowherb, small flo...	14267909	1
Caelo	Willowherb, small flo...	10326104	5
Caelo	Willowherb, small flo...	13200201	3
Caelo	Willowherb, small flo...	13200202-3481312102	1
Caelo	Willowherb, small flo...	10326108	14
Caelo	Willowherb, small flo...	12117701-3371319012	1
Galke	Willowherb, small flo...	47502	1
Galke	Willowherb, small flo...	22347	4
Klenk	Willowherb, small flo...	4721C2120321	1
Hepart AG	Willowherb, small flo...	10326110	2
Klenk	Willowherb, small flo...	C120321	1
Klenk	Willowherb, small flo...	A120418	1

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Supplier	Substance	Batch	Spectra
Klenk	Willowherb, small flo...	4721B130528	1
Klenk	Willowherb, small flo...	4721A101010	2
Klenk	Willowherb, small flo...	4721C120321	10
Klenk	Willowherb, small flo...	4721A120418	11
Klenk	Willowherb, small flo...	4721C110701	4
Klenk	Willowherb, small flo...	4721C130618	4
Klenk	Willowherb, small flo...	4721A120903	7
Klenk	Willowherb, small flo...	2512U-01641	1
Caelo	Willowherb, small flo...	12117701	8
Bahnhof-Apotheke	Wormwood herb, cut	17-121107	1
Bombastus	Wormwood herb, cut	281000	1
Bombastus	Wormwood herb, cut	265417	2
Bombastus	Wormwood herb, cut	221868	1
Caelo	Wormwood herb, cut	11285802	2
Caelo	Wormwood herb, cut	11285810	6
Caelo	Wormwood herb, cut	6101203	1
Caelo	Wormwood herb, cut	12355801	20
Caelo	Wormwood herb, cut	7031301	1
Caelo	Wormwood herb, cut	12355807	10
Caelo	Wormwood herb, cut	13174401	3
Caelo	Wormwood herb, cut	7011401	1
Caelo	Wormwood herb, cut	13381902	3
Caelo	Wormwood herb, cut	13381905	1
Caelo	Wormwood herb, cut	15408304	1
Caelo	Wormwood herb, cut	13174402	2
Caelo	Wormwood herb, cut	11285805	2
Caelo	Wormwood herb, cut	12355804	8
Caelo	Wormwood herb, cut	12355802	3
Caelo	Wormwood herb, cut	12355805	4
Caelo	Wormwood herb, cut	12355808	2
Caelo	Wormwood herb, cut	11285803	1
Caelo	Wormwood herb, cut	272957	1
Caelo	Wormwood herb, cut	277513	1
Galke	Wormwood herb, cut	21330	1
Gehe	Wormwood herb, cut	11285811	1
Gehe	Wormwood herb, cut	13381901	1
Klenk	Wormwood herb, cut	3461A121130	2
Klenk	Wormwood herb, cut	3461A110324	2
Klenk	Wormwood herb, cut	A110324	1
Klenk	Wormwood herb, cut	3461A1100324	1
Phoenix	Wormwood herb, cut	12103003	8
Phönix	Wormwood herb, cut	12355806	7
Sanacorp	Wormwood herb, cut	12103002	2
Caelo	Wormwood herb, cut	12355803	27
Klenk	Yarrow flower, rubbed	4181A121130	1
Caelo	Yarrow flower, rubbed	12267702	1
Caelo	Yarrow flower, rubbed	12363005	5
Caelo	Yarrow flower, rubbed	13350507	1
Caelo	Yarrow flower, rubbed	12267703	2
Caelo	Yarrow flower, rubbed	12363002	6
Caelo	Yarrow flower, rubbed	12338306	1
Caelo	Yarrow flower, rubbed	70139427	1
Klenk	Yarrow flower, rubbed	A110816	3
Alfred Galke	Yarrow herb, cut	19861	1
Anzag 12.11.12 ek:3,85	Yarrow herb, cut	11280513	1
Bahnhof-Apotheke	Yarrow herb, cut	7-121011	1
Bombastus	Yarrow herb, cut	274610	2
Bombastus	Yarrow herb, cut	276498	1
Bombastus	Yarrow herb, cut	274284	1
Bombastus	Yarrow herb, cut	15006702	1

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Supplier	Substance	Batch	Spectra
Bombastus	Yarrow herb, cut	275964	1
Caelo	Yarrow herb, cut	10101205	1
Caelo	Yarrow herb, cut	11218404	1
Caelo	Yarrow herb, cut	11280517	1
Caelo	Yarrow herb, cut	11280511	2
Caelo	Yarrow herb, cut	11306301	1
Caelo	Yarrow herb, cut	12338304	15
Caelo	Yarrow herb, cut	12338305	7
Caelo	Yarrow herb, cut	5021302	1
Caelo	Yarrow herb, cut	12379602	9
Caelo	Yarrow herb, cut	12379603	7
Caelo	Yarrow herb, cut	12338311	2
Caelo	Yarrow herb, cut	12041302	1
Caelo	Yarrow herb, cut	16041302	1
Caelo	Yarrow herb, cut	H-220313-1	1
Caelo	Yarrow herb, cut	13029104	5
Caelo	Yarrow herb, cut	29071301	1
Caelo	Yarrow herb, cut	10081301	1
Caelo	Yarrow herb, cut	13029106	10
Caelo	Yarrow herb, cut	13029105	4
Caelo	Yarrow herb, cut	9101311	1
Caelo	Yarrow herb, cut	16102013E	1
Caelo	Yarrow herb, cut	12379606	9
Caelo	Yarrow herb, cut	9121304	1
Caelo	Yarrow herb, cut	12379607	1
Caelo	Yarrow herb, cut	8011421	1
Caelo	Yarrow herb, cut	27011404	1
Caelo	Yarrow herb, cut	13381810	1
Caelo	Yarrow herb, cut	13381805	1
Caelo	Yarrow herb, cut	14018503	2
Caelo	Yarrow herb, cut	1408510	1
Caelo	Yarrow herb, cut	15006713	1
Caelo	Yarrow herb, cut	15006720	1
Caelo	Yarrow herb, cut	15006708	1
Caelo	Yarrow herb, cut	13029108	9
Caelo	Yarrow herb, cut	12336306	1
Caelo	Yarrow herb, cut	13029103	13
Caelo	Yarrow herb, cut	11280514	2
Caelo	Yarrow herb, cut	12338306-3358319071	1
Caelo	Yarrow herb, cut	1309106	1
Caelo	Yarrow herb, cut	11280512	9
Caelo	Yarrow herb, cut	12338303	10
Caelo	Yarrow herb, cut	12379601	9
Caelo	Yarrow herb, cut	13029107-3418310182	1
Caelo	Yarrow herb, cut	13029107-3436311151	1
Caelo	Yarrow herb, cut	13381806	2
Caelo	Yarrow herb, cut	130929105	1
Caesar & Lorenz	Yarrow herb, cut	12379605	3
Caesar & Loretz GmbH,...	Yarrow herb, cut	11306303	1
Caesar & Loretz GmbH,...	Yarrow herb, cut	12338306	3
Fagron	Yarrow herb, cut	3613M-0165	1
Galke	Yarrow herb, cut	21295	2
Galke	Yarrow herb, cut	22048	7
Galke	Yarrow herb, cut	23318	1
Galke	Yarrow herb, cut	23735	1
Gehe	Yarrow herb, cut	1128503	1
Gehe	Yarrow herb, cut	4181A111122	5
Gehe	Yarrow herb, cut	279023	3
Klenk	Yarrow herb, cut	15333007	1
Klenk	Yarrow herb, cut	4181A101102	1

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Supplier	Substance	Batch	Spectra
Klenk	Yarrow herb, cut	4181A110111	15
Klenk	Yarrow herb, cut	A130709	1
Klenk	Yarrow herb, cut	4181A130710	1
Klenk	Yarrow herb, cut	4181130709	1
Klenk	Yarrow herb, cut	4181B130709	2
Klenk	Yarrow herb, cut	4181a11011	1
Klenk	Yarrow herb, cut	4181a130513	1
Klenk	Yarrow herb, cut	4181A121130	12
nachprüfung	Yarrow herb, cut	C1320	1
Noweda	Yarrow herb, cut	12378603	1
Noweda	Yarrow herb, cut	13381804	2
Phagron	Yarrow herb, cut		3
Phönix	Yarrow herb, cut	4181A130513	10
Wolf	Yarrow herb, cut	230010	1
Wolf	Yarrow herb, cut	B230010	9
Caelo	Yellow chaste weed, cut	1024407	1
Caelo	Yellow chaste weed, cut	10244407	1
Caelo	Yellow chaste weed, cut	12170605	2
Caelo	Yellow chaste weed, cut	15029505	1
Caelo	Yellow chaste weed, cut	11293101	4
Caelo	Yellow chaste weed, cut	512U-01473	1
Caelo	Yellow chaste weed, cut	12170603	1
Klenk	Yellow chaste weed, cut	1591A110511	13
Klenk	Yellow chaste weed, cut	1591A-110511	1
Caelo	Yellow chaste weed, cut	12170602	2
VDL	Yellow chaste weed, cut	10244406	1
Caelo	Zedoary root, cut	11091603	1
Caelo	Zedoary root, cut	13010104	1
Caelo	Zedoary root, cut	25111304	1
Caelo	Zedoary root, cut	12125301	3
Caelo	Zedoary root, cut	13010102	3
Caelo	Zedoary root, cut	12125304	2
Klenk	Zedoary root, cut	6941B121025	3
Klenk	Zedoary root, cut	6941B110329	2
Noweda	Zedoary root, cut	11091605	3
Caelo	Zedoary root, cut	111091607	1
vedono	Zedoary root, cut	13010106	3
Caelo	Zedoary root, powdered	12007504	1
Caelo	Zedoary root, powdered	13165501	2
Caelo	Zedoary root, powdered	13165504	4
Caelo	Zedoary root, powdered	15277101	1
Caelo	Zedoary root, powdered	15352606	1
Klenk	Zedoary root, powdered	12007505	1
Ichtyol/Phönix	Zinc orotate dihydrate	12B02-N02	1
Caelo	Zinc sulfate heptahyd...	11095601	1
Caelo	Zinc sulfate heptahyd...	81554199	1
Caelo	Zinc sulfate heptahyd...	11095621	1
Caelo	Zinc sulfate heptahyd...	12257802	1
Caelo	Zinc sulfate heptahyd...	12257809	2
Caelo	Zinc sulfate heptahyd...	12257816	1
Caelo	Zinc sulfate heptahyd...	4012Q-02798	1
Caelo	Zinc sulfate heptahyd...	12257818	1
Euro OTC	Zinc sulfate heptahyd...	1201031-01	1
Euro OTC	Zinc sulfate heptahyd...	1105002-01	1
Euro OTC	Zinc sulfate heptahyd...	1309011_0	1
Euro OTC	Zinc sulfate heptahyd...	1201031-02	1
Euro OTC	Zinc sulfate heptahyd...	1201031-2	1

Appendix D: Requirements of validation

In order to ensure adherence to the safe scientific status, the individual methods for manufacturing and testing must be validated under certain circumstances (compare § 34 para. 1 no. 3, § 35 para. 1 no. 4 and para. 4 sentence 1 no. 2 b, para. 6 sentence 3 *ApoBetrO* [Pharmacies Rules and Regulations]). The *ApoBetrO* [Pharmacies Rules and Regulations] incorporates a legal definition in § 1 a para. 16 (quotation translated):

“Validation is the provision of documented proof which with a high degree of safety documents that, via a specific process or standard work process, a medicinal product is manufactured and tested, which is in accordance with previously determined quality features.”

Validation documentation can be used to prove that methods or devices which are not described in the Pharmacopoeia within the meaning of § 6 para. 1 sentence 3 *ApBetrO* [Pharmacies Rules and Regulations] achieve the same results as those in the Pharmacopoeia. On the other hand, with the requirements of the demanded validation it must be observed whether the respective testing method is already incorporated in the Pharmacopoeia.

NIR spectroscopy as a general testing method need not be validated in accordance with the express ruling in the *Ph. Eur. Section 1.1* [3], as it is already described in *Section 2.2.40* of the *Ph. Eur.* as an area of application for the identification of raw materials.

However, a special validation requirement exists for the reference database. This requirement is met with the existing document. Further requirements or rules as to how this proof must be furnished do not exist. It is required that the processes guarantee the same results as the methods and devices in the Pharmacopoeia [17].

Carrying out identity tests with *Apo-Ident* is therefore also possible if the NIR spectroscopy process is not required in the Pharmacopoeia monograph of the substance for identity testing. All NIR analyses with *Apo-Ident* prove several, often all molecule groups and are therefore comparable with a series of individual, targeted chemical proofs [4]. Therefore, the identity proof with *Apo-Ident* replaces the monograph test series (with two or more test combinations).

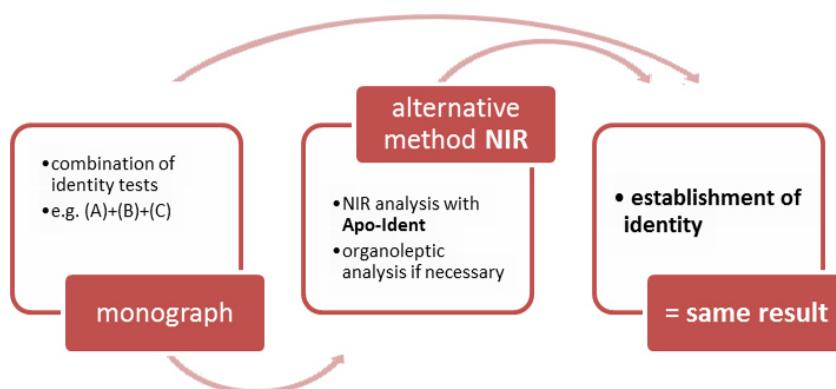


Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

With this validation documentation, proof is furnished that identical results are achieved with *Apo-Ident* and Pharmacopoeia methods, i.e. confirmation of the identity of the raw material [2].

Appendix E: Conformity of Apo-Ident with the European pharmacopeia

According to *Ph. Eur. Section 2.2.40*, NIR spectroscopy is basically suitable for: “Identification of agents, excipients, dosage forms, intermediate manufacturing products, chemical raw materials and packaging materials” ([3], quotation translated).

The fact that *Apo-Ident* meets the further criteria of the European Pharmacopoeia under the headings in *Section 2.2.40*

- Apparatus
- Measurement methods
- Sample preparation and presentation
- Testing the functionality of the instrument
- Identification and characterisation (qualitative analysis)
- Quantitative analysis
- Ongoing model evaluation
- Transfer of databases
- Data storage

can be proven based on the *HiperScan GmbH* documentation of “Meeting 2.2.40 *Ph. Eur.* by *Apo-Ident*” [4].

Appendix F: Addition to the second-stage models

As described in the general part of the *Apo-Ident* validation documentation, in the section [Model creation procedure and validation runs](#), under 2. *Generating the chemometric models (calibration) in f)*, it is possible to create a further chemometric model for certain substances (second-stage model) and to undertake the assessment in several steps.

Substances in second-stage models

In the substance class *APIs & excipients, solid*, a distinction is made between the following substances in the listed second-stage models:

Submodell - Submodel 1

[Betamethasone valerate](#)
[Betamethasone, micronized](#)
[Budesonide, micronized](#)
[Capsaicin](#)
[Dexamethasone](#)
[Erythromycin](#)
[Heparin sodium](#)
[Norethisterone acetate](#)
[Prednicarbate, micronized](#)
[Prednisolone, micronized](#)
[Prednisone](#)
[Triamcinolone acetonide](#)
[Triamcinolone, micronized](#)

Submodell - Submodel 2

[Beclometasone dipropionate](#)
[Betamethasone dipropionate, micronized](#)
[Clobetasol propionate](#)
[Gentamicin sulfate](#)
[Oxybutynin hydrochloride](#)
[Sodium benzoate](#)
[Sodium citrate](#)

Submodell - Submodel 3

[Alfatradiol](#)
[Estriol](#)
[Pregnenolone](#)
[Progesterone, micronized](#)
[Quinine hydrochloride](#)
[Quinine sulfate](#)
[Spironolactone](#)
[Testosterone propionate](#)

Submodell - Submodel 4

[Bacitracin](#)
[Calcium citrate tetrahydrate](#)
[Cyanocobalamin](#)
[Ethinylestradiol](#)

Methylcobalamin

Submodell - Submodel 5

Fusidic acid
Povidone 25, soluble
Povidone iodine

Submodell - Submodel 7

Acetylcysteine
Bismuth gallath, basic
Folic acid hydrate

Submodell - Submodel 8

Eosin Y
Quinoline yellow
Saccharin sodium

Submodell - Submodel 9

Chlortetracycline hydrochloride
Ethacridine lactate monohydrate
Levothyroxin sodium
Vancomycin hydrochloride

References

- [1] ABDA – BUNDESVEREINIGUNG DEUTSCHER APOTHEKERVERBÄNDE: Verordnung über den Betrieb von Apotheken (Apothekenbetriebsordnung – ApBetrO), 2012
- [2] REIMANN, B. ; REGIERUNGSPRÄSIDIUM DARMSTADT: Hinweise zur ordnungsgemäßen Prüfung von Arzneimitteln und Ausgangsstoffen (§§ 6 und 11 *ApBetrO*), 2007
- [3] *Europäisches Arzneibuch, Grundwerk 2017*. 9. Ausgabe. Deutscher Apotheker Verlag (978-3-7692-6679-5)
- [4] HIPERSCAN GMBH: Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident, 2013
- [5] ARBEITSGEMEINSCHAFT DER PHARMAZIERÄTE DEUTSCHLANDS (APD): Resolution in Verbindung mit §§ 6 und 11 *ApBetrO* Verwendung eines Nah-Infrarot-Spektrometers (NIR) zur Identitätsprüfung, 16. 10. 2013, DAZ 48, November 2013
- [6] ARBEITSGEMEINSCHAFT DER PHARMAZIERÄTE DEUTSCHLANDS (APD): Resolution 2014, Arbeitsgemeinschaft der Pharmazieräte Deutschlands (APD), Oktober 2014
- [7] *DAC/NRF*. Govi-Verlag (978-3-7741-0044-2)
- [8] KESSLER, W.: *Multivariate Datenanalyse*. WILEY-VCH Verlag, 2007 (978-3-527-31262-7)
- [9] NÆS, T. ; ISAKSSON, T. ; FEARN, T. ; DAVIES, T.: *Multivariate Calibration and Classification*. NIR Publications, 2002 (978 0 9528666 2 6)
- [10] HANLEY, J. A. ; LIPPMAN-HAND, A.: If nothing goes wrong, is everything all right? In: *Journal of the American Medical Association* 249 (1983), S. 1743–1745
- [11] JOVANOVIĆ, B. D. ; LEVY, P. S.: A Look at the Rule of Three. In: *The American Statistician* 51 (1997), S. 137–139
- [12] BRONSTEIN, I. N. ; SEMENDJAJEW, K. A. ; MUSIOL, G. ; MÜHLIG, H.: *Taschenbuch der Mathematik*. 5. überarbeitete und erweiterte Auflage. Verlag Harri Deutsch, 2000 (3-8171-2015-2)
- [13] MAHALANOBIS, P.: On the generalized distance in statistics. In: *Proc. Nat. Inst. Sci. India (Calcutta)* 2 (1936), S. 49–55
- [14] YAMBOR, B. ; DRAPER, W. ; BEVERIDGE, R.: Analyzing PCA-based face recognition algorithms: Eigenvector selection and distance measures. In: *Second Workshop Empirical Evaluation in Computer Vision* (2000)
- [15] HIPERSCAN GMBH: Identifikationsmethodik Apo-Ident, 2012
- [16] HIPERSCAN GMBH: Datenvorbehandlung des Identifikationssystems Apo-Ident, 2012
- [17] CYRAN ; RÖTTA: Apothekenbetriebsordnung, Kommentar § 6 Rn. 10, 2010

Index

- 5-aminolevulinic acid hydrochloride, [23](#)
- Acacia, dried dispersion, [29](#)
- Acaciae gummi dispersione desiccatum, *see*
Acacia, dried dispersion, [29](#)
- Acetylcysteine, [35](#)
- Acetylcysteinum, *see* Acetylcysteine, [35](#)
- Acetylsalicylic acid, [41](#)
- Aciclovir, [47](#)
- Aciclovirum, *see* Aciclovir, [47](#)
- Acidum acetylsalicylicum, *see* Acetylsalicylic acid, [41](#)
- Acidum aminolaevulinicum hydrochloricum, *see* 5-aminolevulinic acid hydrochloride, [23](#)
- Acidum ascorbinicum, *see* Ascorbic acid, [115](#)
- Acidum benzoicum, *see* Benzoic acid, [153](#)
- Acidum boricum, *see* Boric acid, [223](#)
- Acidum citricum, *see* Citric acid, [425](#)
- Acidum citricum monohydricum, *see* Citric acid monohydrate, [441](#)
- Acidum folicum hydricum, *see* Folic acid hydrate, [731](#)
- Acidum fusidicum, *see* Fusidic acid, [753](#)
- Acidum glutaminicum, *see* Glutamic acid, [803](#)
- Acidum nicotinicum, *see* Nicotinic acid, [1329](#)
- Acidum oxalicum cryst., *see* Oxalic acid, [1381](#)
- Acidum salicylicum, *see* Salicylic acid, [1709](#)
- Acidum sorbicum, *see* Sorbic acid, [1805](#)
- Acidum stearicum, *see* Stearic acid 50, [1841](#)
- Acidum tartaricum, *see* Tartaric acid, [1883](#)
- Acidum tranexamicum, *see* Tranexamic acid, [1977](#)
- Acidum-(L)-malicum, *see* L-malic acid, [1035](#)
- Adeps solidus, *see* Waxes / Fats, [2107](#)
- Adeps solidus W35, *see* Waxes / Fats, [2107](#)
- Adrenaline hydrogen tartrate, *see*
Epinephrine hydrogen tartrate, [631](#)
- Adrenolini tartras, *see* Epinephrine hydrogen tartrate, [631](#)
- Aescinum solubile, *see* Escin, water-soluble, [655](#)
- Albendazole, [51](#)
- Albendazolum, *see* Albendazole, [51](#)
- Alcohol cetylicus, *see* Cetostearyl alcohol, [339](#)
- Alcohol cetylicus et stearylicus, *see*
Cetostearyl alcohol, [339](#)
- Alcohol cetylicus et stearylicus emulsificans A, *see* Cetostearyl alcohol, [339](#)
- Alcoholes emulsificantes nonionici, *see*
Non-ionic emulsifying alcohol, [1333](#)
- Alcoholes lanae, *see* Wool alcohols, [2129](#)
- Alfatradiol, [55](#)
- Alfatradiolum, *see* Alfatradiol, [55](#)
- Allantoin, [63](#)
- Allantoinum, *see* Allantoin, [63](#)
- Allopurinol, [69](#)
- Allopurinolum, *see* Allopurinol, [69](#)
- alpha-Tocopherolum aceticum siccatum, *see*
alpha-tocopheryl acetate dry concentrate, [73](#)
- alpha-tocopheryl acetate dry concentrate, [73](#)
- Ambroxol hydrochloride, [79](#)
- Ambroxoli hydrochloridum, *see* Ambroxol hydrochloride, [79](#)
- Amifampridine, [85](#)
- Amifampridinum, *see* Amifampridine, [85](#)
- Amitriptyline hydrochloride, [91](#)
- Amitriptylini hydrochloridum, *see*
Amitriptyline hydrochloride, [91](#)
- Amphotericin B, [97](#)
- Amphotericinum B, *see* Amphotericin B, [97](#)
- Amylum Maydis, *see* Starch, [1833](#)
- Amylum oryzae, *see* Starch, [1833](#)
- Amylum Solani, *see* Starch, [1833](#)
- Amylum tritici, *see* Starch, [1833](#)
- Arginine, [103](#)
- Arginine hydrochloride, [109](#)
- Arginini hydrochloridum, *see* Arginine hydrochloride, [109](#)
- Argininum, *see* Arginine, [103](#)
- Ascorbic acid, [115](#)
- Ascorbyl palmitate, [121](#)
- Ascorbylis palmitas, *see* Ascorbyl palmitate, [121](#)
- Atropine sulfate, [127](#)
- Atropine sulphate, *see* Atropine sulfate, [127](#)
- Atropini sulfas, *see* Atropine sulfate, [127](#)
- Bacitracin, [133](#)
- Bacitracinum, *see* Bacitracin, [133](#)
- Beclometasone dipropionate, [139](#)
- Beclometasoni dipropionas, *see*
Beclometasone dipropionate, [139](#)
- Benzocaine, [145](#)
- Benzocainum, *see* Benzocaine, [145](#)
- Benzoic acid, [153](#)
- Benzydamine hydrochloride, [159](#)
- Benzydamini hydrochloridum, *see*
Benzydamine hydrochloride, [159](#)
- Betaine monohydrate, [165](#)
- Betainum monohydricum, *see* Betaine monohydrate, [165](#)
- Betamethasone dipropionate, micronized, [169](#)
- Betamethasone valerate, [179](#)
- Betamethasone, micronized, [197](#)
- Betamethasoni dipropionas micronisatum, *see*
Betamethasone dipropionate,

- micronized, [169](#)
- Betamethasoni valeras, *see* Betamethasone valerate, [179](#)
- Betamethasonum, micronisatum, *see* Betamethasone, micronized, [197](#)
- Bifonazole, [203](#)
- Bifonazolum, *see* Bifonazole, [203](#)
- Biotin, [209](#)
- Biotinum, *see* Biotin, [209](#)
- Bismuth gallath, basic, [215](#)
- Bismuthi subgallas, *see* Bismuth gallath, basic, [215](#)
- Borax, *see* Sodium tetraborate, [1799](#)
- Boric acid, [223](#)
- Budesonide, micronized, [229](#)
- Budesonidum micronisatum, *see* Budesonide, micronized, [229](#)
- Butylated hydroxytoluene, [237](#)
- Butylhydroxytoluenum, *see* Butylated hydroxytoluene, [237](#)
- Caffeine, [245](#)
- Calcii ascorbinicum, *see* Calcium ascorbate, [251](#)
- Calcii citras tetrahydricus, *see* Calcium citrate tetrahydrate, [257](#)
- Calcii ethylhydrogenfumaras, *see* Ethyl hydrogen fumarate calcium, [707](#)
- Calcii gluconas, *see* Calcium gluconate, [263](#)
- Calcii glycerophosphas, *see* Calcium glycerophosphate, [271](#)
- Calcii lactas pentahydricus, *see* Calcium lactate pentahydrate, [277](#)
- Calcii orotas dihydricus, *see* Calcium orotate dihydrate, [283](#)
- Calcii panthothenicum, *see* Calcium pantothenate, [289](#)
- Calcium ascorbate, [251](#)
- Calcium citrate tetrahydrate, [257](#)
- Calcium gluconate, [263](#)
- Calcium glycerophosphate, [271](#)
- Calcium lactate pentahydrate, [277](#)
- Calcium orotate dihydrate, [283](#)
- Calcium pantothenate, [289](#)
- Camphor, racemic, [295](#)
- Cannabidiol, [299](#)
- Capsaicin, [305](#)
- Capsaicinoida, *see* Capsaicin, [305](#)
- Captopril, [311](#)
- Captoprilum, *see* Captopril, [311](#)
- Carbamidum, *see* Urea, [2069](#)
- Carbomers 35000 / 50000, [319](#)
- Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s), [327](#)
- Carmellosum natricum (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s), *see* Carmellose sodium (400 / 450 / 500 / 600 / 1600 / 2000 mPa · s), [327](#)
- Cellulose, microcrystalline, [333](#)
- Cellulosum microcristallinum, *see* Cellulose, microcrystalline, [333](#)
- Cera alba, *see* Waxes / Fats, [2107](#)
- Cera flava, *see* Waxes / Fats, [2107](#)
- Cetomacrogol emulsifying wax 1000 NI, *see* Cetostearyl alcohol, [339](#)
- Cetostearyl alcohol, [339](#)
- Cetyl alcohol, *see* Cetostearyl alcohol, [339](#)
- Cetyl palmitate 15, *see* Waxes / Fats, [2107](#)
- Cetylis palmitas 15, *see* Waxes / Fats, [2107](#)
- Chinidini sulfas, *see* Quinidine sulfate dihydrate, [1649](#)
- Chinini dihydrochloridum, *see* Quinine dihydrochloride, [1653](#)
- Chinini hydrochloridum, *see* Quinine hydrochloride, [1657](#)
- Chinini sulfas, *see* Quinine sulfate, [1663](#)
- Chinolini et kalii sulfas, *see* Quinolinol sulfate potassium sulfate, [1673](#)
- Chloral hydrate, [351](#)
- Chlorali hydras, *see* Chloral hydrate, [351](#)
- Chloramphenicol, [359](#)
- Chloramphenicolum, *see* Chloramphenicol, [359](#)
- Chlorhexidine diacetate, [371](#)
- Chlorhexidini acetas, *see* Chlorhexidine diacetate, [371](#)
- Chlorocresol, [379](#)
- Chlorocresolum, *see* Chlorocresol, [379](#)
- Chlortetracycline hydrochloride, [385](#)
- Chlortetracyclini hydrochloridum, *see* Chlortetracycline hydrochloride, [385](#)
- Cholesterol, [391](#)
- Cholesterolum, *see* Cholesterol, [391](#)
- Choline chloride, [397](#)
- Choline hydrogen tartrate, [401](#)
- Cholinii chloridum, *see* Choline chloride, [397](#)
- Cholinium bitartaricum, *see* Choline hydrogen tartrate, [401](#)
- Ciclopirox olamine, [407](#)
- Ciclopirox alaminum, *see* Ciclopirox olamine, [407](#)
- Ciclosporin, [413](#)
- Ciclosporinum, *see* Ciclosporin, [413](#)
- Ciprofloxacin hydrochloride, [421](#)
- Ciprofloxacini hydrochloridum, *see* Ciprofloxacin hydrochloride, [421](#)
- Citric acid, [425](#)
- Citric acid monohydrate, [441](#)
- Citrulline, [447](#)
- Citrullinum, *see* Citrulline, [447](#)
- Clindamycin hydrochloride, [453](#)
- Clindamycini hydrochloridum, *see* Clindamycin hydrochloride, [453](#)
- Clioquinol, [461](#)

- Clioquinolum, *see* Clioquinol, [461](#)
Clobetasol propionate, [471](#)
Clobetasoli propionas, *see* Clobetasol propionate, [471](#)
Clonidine hydrochloride, [485](#)
Clonidini hydrochloridum, *see* Clonidine hydrochloride, [485](#)
Clotrimazole, [489](#)
Clotrimazolum, *see* Clotrimazole, [489](#)
Cocoa butter, *see* Waxes / Fats, [2107](#)
Coffeinum, *see* Caffeine, [245](#)
Colistin sulfate, [507](#)
Colistin sulphate, *see* Colistin sulfate, [507](#)
Colistini sulfas, *see* Colistin sulfate, [507](#)
Corn starch, *see* Starch, [1833](#)
Cromolyn sodium, *see* Sodium cromoglicate, [1769](#)
Cyanocobalamin, [513](#)
Cyanocobalaminum, *see* Cyanocobalamin, [513](#)
Cyproterone acetate, [519](#)
Cyproteroni acetat, *see* Cyproterone acetate, [519](#)
Cystine, [525](#)
Cystinum, *see* Cystine, [525](#)
- D-Galactopyranose, *see* Galactose, [759](#)
Dapsone, [529](#)
Dapsonum, *see* Dapsone, [529](#)
Dequalinii chloridum, *see* Dequalinium chloride, [533](#)
Dequalinium chloride, [533](#)
Dexamethasone, [541](#)
Dexamethasone acetate, [553](#)
Dexamethasoni acetat, *see* Dexamethasone acetate, [553](#)
Dexamethasonum, *see* Dexamethasone, [541](#)
Dextromethorphan hydrobromide monohydrate, [559](#)
Dextromethorphani hydrobromidum, *see* Dextromethorphan hydrobromide monohydrate, [559](#)
Diclofenac sodium, [563](#)
Diclofenacum natricum, *see* Diclofenac sodium, [563](#)
Diltiazem hydrochloride, [571](#)
Diltiazemi hydrochloridum, *see* Diltiazem hydrochloride, [571](#)
Dimethyl fumarate, [585](#)
Dinatrii edetas, *see* Sodium edetate, [1781](#)
Diphenhydramine hydrochloride, [589](#)
Diphenhydramini hydrochloridum, *see* Diphenhydramine hydrochloride, [589](#)
Dithranol, [595](#)
Dithranolum, *see* Dithranol, [595](#)
Doxycycline hyclate, [603](#)
Doxycyclini hyclas, *see* Doxycycline hyclate, [603](#)
Doxylamine hydrogen succinate, [609](#)
Doxylamine succinate, *see* Doxylamine hydrogen succinate, [609](#)
Doxylamini hydrogenosuccinas, *see* Doxylamine hydrogen succinate, [609](#)
- Emulsifying cetostearyl alcohol (type A), *see* Cetostearyl alcohol, [339](#)
Enalapril maleate, [615](#)
Enalapriili maleas, *see* Enalapril maleate, [615](#)
Eosin Y, [619](#)
Eosinum natricum, *see* Eosin Y, [619](#)
Ephedrine hydrochloride, [625](#)
Ephedrini hydrochloridum, *see* Ephedrine hydrochloride, [625](#)
Epinephrine hydrogen tartrate, [631](#)
Erythromycin, [637](#)
Erythromycinum, *see* Erythromycin, [637](#)
Escin, water-soluble, [655](#)
Estradiol benzoate, [659](#)
Estradiol hemihydrate, [667](#)
Estradiol valerate, [675](#)
Estradioli benzoas, *see* Estradiol benzoate, [659](#)
Estradioli valeras, *see* Estradiol valerate, [675](#)
Estradiolum hemihydricum, *see* Estradiol hemihydrate, [667](#)
Estriol, [683](#)
Estriolum, *see* Estriol, [683](#)
Ethacridine lactate monohydrate, [691](#)
Ethacridini lactas monohydricus, *see* Ethacridine lactate monohydrate, [691](#)
Ethinylestradiol, [697](#)
Ethinylestradiolum, *see* Ethinylestradiol, [697](#)
Ethosuximide, [703](#)
Ethosuximidum, *see* Ethosuximide, [703](#)
Ethyl hydrogen fumarate calcium, [707](#)
- Fampridine, [713](#)
Fampridinum, *see* Fampridine, [713](#)
Finasteride (form III), [719](#)
Finasteridum (Form III), *see* Finasteride (form III), [719](#)
Fluocinolone acetate, micronized, [725](#)
Fluocinoloni acetamidum micron., *see* Fluocinolone acetate, micronized, [725](#)
Folic acid hydrate, [731](#)
Fructose, [737](#)
Fructosum, *see* Fructose, [737](#)
Furosemide, [747](#)
Furosemidum, *see* Furosemide, [747](#)
Fusidic acid, [753](#)
- Galactose, [759](#)

- Gelatina alba, *see* Gelatine, white, [765](#)
 Gelatine, white, [765](#)
 Gentamicin sulfate, [771](#)
 Gentamicin sulphate, *see* Gentamicin sulfate, [771](#)
 Gentamicini sulfas, *see* Gentamicin sulfate, [771](#)
 Glucose, [783](#)
 Glucose monohydrate, [791](#)
 Glucosum, *see* Glucose, [783](#)
 Glucosum monohydricum, *see* Glucose monohydrate, [791](#)
 Glutamic acid, [803](#)
 Glutamine, [807](#)
 Glutaminum, *see* Glutamine, [807](#)
 Glycerol monostearate 40-55%, *see* Monostereates, [1277](#)
 Glycerol monostearate 60, *see* Monostereates, [1277](#)
 Glycerol monostearate, emulsifying, *see* Monostereates, [1277](#)
 Glyceroli monostearates 40-55%, *see* Monostereates, [1277](#)
 Glyceroli monostearates 60, *see* Monostereates, [1277](#)
 Glyceroli monostearates emulsificantes, *see* Monostereates, [1277](#)
 Glycine, [811](#)
 Glycinum, *see* Glycine, [811](#)
 Glycopyrronii bromidum, *see* Glycopyrronium bromide, [817](#)
 Glycopyrronium bromide, [817](#)
 Gramicidin, [821](#)
 Gramicidinum, *see* Gramicidin, [821](#)
 Griseofulvin, [827](#)
 Griseofulvinum, *see* Griseofulvin, [827](#)
 Guaifenesin, [833](#)
 Guaifenesinum, *see* Guaifenesin, [833](#)
- Hard fat in pastilles, *see* Waxes / Fats, [2107](#)
 Hard fat W35, *see* Waxes / Fats, [2107](#)
 Heparin sodium, [839](#)
 Heparinum natricum, *see* Heparin sodium, [839](#)
 Histamine dihydrochloride, [845](#)
 Histamini dihydrochloridum, *see* Histamine dihydrochloride, [845](#)
 Histidine, [851](#)
 Histidinum, *see* Histidine, [851](#)
 Hyaluronic acid sodium salt, [855](#)
 Hydrochinonum, *see* Hydroquinone, [893](#)
 Hydrochlorothiazide, [859](#)
 Hydrochlorothiazidum, *see* Hydrochlorothiazide, [859](#)
 Hydrocortisone, [865](#)
 Hydrocortisone acetate, [879](#)
 Hydrocortisoni acetas, *see* Hydrocortisone acetate, [879](#)
 Hydrocortisonum purum, *see* Hydrocortisone, [865](#)
 Hydroquinone, [893](#)
 Hydroxyethylcellulose (apparent viscosity 300 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulose (apparent viscosity 5000 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulose (apparent viscosity 9000 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulose (nominal viscosity 300 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulose (nominal viscosity 5000 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulose (nominal viscosity 9000 mPas), *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulosum 250 M, *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulosum G 300, *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxyethylcellulosum HX, *see* Hydroxyethylcelluloses (300 / 5000/ 9000 mPa · s), [899](#)
 Hydroxypropylcellulose (300 mPa · s), *see* Methylcellulose, [1193](#)
 Hydroxypropylcellulosum (300 mPa · s), *see* Methylcellulose, [1193](#)
 Hyoscine butylbromide, [913](#)
 Hyoscine hydrobromide, [917](#)
 Hyoscini butylbromidum, *see* Hyoscine butylbromide, [913](#)
 Hypromellose 4000, *see* Methylcellulose, [1193](#)
 Hypromellosum E4M Prem, *see* Methylcellulose, [1193](#)
- Ibuprofen, [923](#)
 Ibuprofenum, *see* Ibuprofen, [923](#)
 Indometacin, [927](#)
 Indometacinum, *see* Indometacin, [927](#)
 Inositol, [933](#)
 Inositolum, *see* Inositol, [933](#)
 Iodoform, [937](#)
 Iodoformium, *see* Iodoform, [937](#)
 Ipratropii bromidum, *see* Ipratropium

- bromide, [943](#)
- Ipratropium bromide, [943](#)
- Isoleucine, [947](#)
- Isoleucinum, *see* Isoleucine, [947](#)
- Isorbidi dinitras 40%, *see* Isosorbide dinitrate 40%, [953](#)
- Isosorbide dinitrate 40%, [953](#)
- Isoxsuprini hydrochloridum, *see* Isoxuprine hydrochloride, [961](#)
- Isoxuprine hydrochloride, [961](#)
- Kalii citras, *see* Potassium citrate, [1477](#)
- Kalii hydrogentartras, *see* Potassium hydrogen tartrate, [1485](#)
- Kalii natrii tartras tetrahydricus, *see* Potassium sodium tartrate tetrahydrate, [1491](#)
- Kalii sorbas, *see* Potassium sorbate, [1495](#)
- Kalii tartras hemihydricus, *see* Potassium tartrate hemihydrate, [1505](#)
- Ketamine hydrochloride, [965](#)
- Ketamini hydrochloridum, *see* Ketamine hydrochloride, [965](#)
- Ketoconazole, [971](#)
- Ketoconazolum, *see* Ketoconazole, [971](#)
- L-citrulline, *see* Citrulline, [447](#)
- L-glutamine, *see* Glutamine, [807](#)
- L-glutathione, [999](#)
- L-Glutathionum, *see* L-glutathione, [999](#)
- L-histidine, *see* Histidine, [851](#)
- L-isoleucine, *see* Isoleucine, [947](#)
- L-leucine, [1031](#)
- L-malic acid, [1035](#)
- L-phenylalanine, [1039](#)
- L-proline, [1045](#)
- L-serine, *see* Serine, [1727](#)
- L-threonine, [1049](#)
- L-tryptophan, [1053](#)
- Lactose monohydrate, [977](#)
- Lactosum monohydricum, *see* Lactose monohydrate, [977](#)
- Lecithinum e sojæ plv., *see* Soy lecithin (instant form), [1819](#)
- Leucinum, *see* L-leucine, [1031](#)
- Levocarnitine, [991](#)
- Levocarnitivum, *see* Levocarnitine, [991](#)
- Levothyroxin sodium, [995](#)
- Levothyroxinum natrii, *see* Levothyroxin sodium, [995](#)
- Lidocaine, [1003](#)
- Lidocaine hydrochloride monohydrate, [1013](#)
- Lidocaini hydrochloridum monohydricum, *see* Lidocaine hydrochloride monohydrate, [1013](#)
- Lidocainum, *see* Lidocaine, [1003](#)
- Lithii orotas monohydricum, *see* Lithium orotate monohydrate, [1027](#)
- Lithium orotate monohydrate, [1027](#)
- Lysine HCl, *see* Lysine hydrochloride, [1059](#)
- Lysine hydrochloride, [1059](#)
- Lysini hydrochloridum, *see* Lysine hydrochloride, [1059](#)
- Macrogols 1500, [1065](#)
- Macrogols 4000, [1071](#)
- Macrogolum 1500, *see* Macrogols 1500, [1065](#)
- Macrogolum 4000, *see* Macrogols 4000, [1071](#)
- Magnesii asparticum tetrahydricum, *see* Magnesium hydrogen aspartate tetrahydrate, [1089](#)
- Magnesii citras, *see* Magnesium citrate, [1083](#)
- Magnesii hydrogenocitras hydricus, *see* Magnesium hydrogen citrate, [1093](#)
- Magnesii oroticum dihydricum, *see* Magnesium orotate dihydrate, [1101](#)
- Magnesii stearas, *see* Magnesium stearate, [1107](#)
- Magnesium citrate, [1083](#)
- Magnesium hydrogen aspartate tetrahydrate, [1089](#)
- Magnesium hydrogen citrate, [1093](#)
- Magnesium hydrogen citrate, hydrated, *see* Magnesium hydrogen citrate, [1093](#)
- Magnesium orotate dihydrate, [1101](#)
- Magnesium stearate, [1107](#)
- Manganese orotate dihydrate, [1113](#)
- Mannitol, [1117](#)
- Mannitolum, *see* Mannitol, [1117](#)
- Melatonin, [1131](#)
- Melatoninum, *see* Melatonin, [1131](#)
- Menthol, [1141](#)
- Mentholum, *see* Menthol, [1141](#)
- Mepivacaine hydrochloride, [1153](#)
- Mepivacaini hydrochloridum, *see* Mepivacaine hydrochloride, [1153](#)
- Mesalazine, [1157](#)
- Mesalazinum, *see* Mesalazine, [1157](#)
- Metamizol sodium monohydrate, [1163](#)
- Metamizolum natricum monohydricum, *see* Metamizol sodium monohydrate, [1163](#)
- Methacholine chloride, [1167](#)
- Methacholinii chloridum, *see* Methacholine chloride, [1167](#)
- Methionine, [1173](#)
- Methioninum, *see* Methionine, [1173](#)
- Methoxsalen, [1179](#)
- Methoxsalenum, *see* Methoxsalen, [1179](#)
- Methyl-4-hydroxybenzoate, [1185](#)
- Methylcellulose, [1193](#)
- Methylcellulosum, *see* Methylcellulose, [1193](#)
- Methylcobalamin, [1201](#)
- Methylis parahydroxybenzoas, *see* Methyl-4-hydroxybenzoate, [1185](#)

- Methylis parahydroxybenzoas natricus, *see*
Sodium methyl-4-hydroxybenzoate,
1789
- Methylprednisolone, 1207
- Methylprednisolonum, *see*
Methylprednisolone, 1207
- Metoclopramide hydrochloride, 1211
- Metoclopramidi hydrochloridum, *see*
Metoclopramide hydrochloride, 1211
- Metoprolol tartrate, 1215
- Metoprololi tartras, *see* Metoprolol tartrate,
1215
- Metronidazole, 1221
- Metronidazolum, *see* Metronidazole, 1221
- Miconazole nitrate, 1239
- Miconazoli nitras, *see* Miconazole nitrate,
1239
- Microcrystalline wax, *see* Waxes / Fats, 2107
- Minoxidil, 1251
- Minoxidilum, *see* Minoxidil, 1251
- Mometasone furoate, micronized, 1265
- Mometasoni furoas micronisatum, *see*
Mometasone furoate, micronized,
1265
- Monostereates, 1277
- Mupirocin calcium, 1285
- Mupirocinum calcii, *see* Mupirocin calcium,
1285
- Naloxone hydrochloride dihydrate, 1289
- Naloxoni hydrochloridum dihydricum, *see*
Naloxone hydrochloride dihydrate,
1289
- Naphazoline hydrochloride, 1295
- Naphazoline nitrate, 1301
- Naphazolini hydrochloridum, *see* Naphazoline
hydrochloride, 1295
- Naphazolini nitras, *see* Naphazoline nitrate,
1301
- Naproxen, 1305
- Naproxenum, *see* Naproxen, 1305
- Natrii acetat trihydricum, *see* Sodium acetate
trihydrate, 1737
- Natrii ascorbas, *see* Sodium ascorbate, 1743
- Natrii benzoas, *see* Sodium benzoate, 1749
- Natrii citras, *see* Sodium citrate, 1757
- Natrii cromoglicas, *see* Sodium cromoglicate,
1769
- Natrii cyclamas, *see* Sodium cyclamate, 1775
- Natrii Hyaluronas, *see* Hyaluronic acid
sodium salt, 855
- Natrii lactoflavini phosphoricum, *see*
Riboflavin phosphate sodium, 1695
- Natrii laurylsulfuricum, *see* Waxes / Fats,
2107
- Natrii salicylas plv., *see* Sodium salicylate,
powdered, 1795
- Neomycin sulfate, 1309
- Neomycin sulphate, *see* Neomycin sulfate,
1309
- Neomycini sulfas, *see* Neomycin sulfate, 1309
- Neostigmine bromide, 1317
- Neostigmini bromidum, *see* Neostigmine
bromide, 1317
- Nicotinamide, 1323
- Nicotinic acid, 1329
- Nicotinoylamidum, *see* Nicotinamide, 1323
- Non-ionic emulsifying alcohol, 1333
- Norethisterone acetate, 1339
- Norethisteroni acetat, *see* Norethisterone
acetate, 1339
- Nystatin, 1345
- Nystatinum, *see* Nystatin, 1345
- Octenidine dihydrochloride, 1353
- Octenidini dihydrochloridum, *see* Octenidine
dihydrochloride, 1353
- Ofloxacin, 1361
- Ofloxacinum, *see* Ofloxacin, 1361
- Oleum cacao, *see* Waxes / Fats, 2107
- Omeprazole, 1367
- Omeprazolum, *see* Omeprazole, 1367
- Ornithine aspartate, 1373
- Ornithine hydrochloride, 1377
- Ornithinum asparticum, *see* Ornithine
aspartate, 1373
- Ornithinum hydrochloricum, *see* Ornithine
hydrochloride, 1377
- Oxalic acid, 1381
- Oxetacaine, 1387
- Oxetacainum, *see* Oxetacaine, 1387
- Oxybuprocaine hydrochloride, 1391
- Oxybuprocaini hydrochloridum, *see*
Oxybuprocaine hydrochloride, 1391
- Oxybutynin hydrochloride, 1397
- Oxybutynini hydrochloridum, *see*
Oxybutynin hydrochloride, 1397
- Oxytetracycline hydrochloride, 1403
- Oxytetracyclini hydrochloridum, *see*
Oxytetracycline hydrochloride, 1403
- Pancreas powder, 1411
- Pancreatis pulvis, *see* Pancreas powder, 1411
- Papaverine hydrochloride, 1415
- Papaverini hydrochloridum, *see* Papaverine
hydrochloride, 1415
- Paracetamol, 1421
- Paracetamolum, *see* Paracetamol, 1421
- Paraffin, hard, *see* Waxes / Fats, 2107
- Paraffin, microcrystalline, *see* Waxes / Fats,
2107
- Paraffinum durum in rotulis, *see* Waxes /
Fats, 2107
- Paraffinum microcristallinum, *see* Waxes /
Fats, 2107

- Patent blue V, [1427](#)
 Phenazone, [1433](#)
 Phenazonum, *see* Phenazone, [1433](#)
 Pheniramine maleate, [1439](#)
 Pheniramini maleas, *see* Pheniramine maleate, [1439](#)
 Phenylalaninum, *see* L-phenylalanine, [1039](#)
 Phenylbutazon, [1445](#)
 Phenylbutazonum, *see* Phenylbutazon, [1445](#)
 Phenylephrine hydrochloride, [1449](#)
 Phenylephrini hydrochloridum, *see* Phenylephrine hydrochloride, [1449](#)
 Phenytoin, [1455](#)
 Phenytoinum, *see* Phenytoin, [1455](#)
 Pilocarpine hydrochloride, [1459](#)
 Pilocarpini hydrochloridum, *see* Pilocarpine hydrochloride, [1459](#)
 Poloxamera, *see* Poloxamers 407, [1465](#)
 Poloxamers 407, [1465](#)
 Polymyxin B sulfate, [1471](#)
 Polymyxin B sulphate, *see* Polymyxin B sulfate, [1471](#)
 Polymyxini B sulfas, *see* Polymyxin B sulfate, [1471](#)
 Potassium citrate, [1477](#)
 Potassium guaiacolsulfonate, *see* Sulfogaiacol hydrate, [1871](#)
 Potassium hydrogen tartrate, [1485](#)
 Potassium sodium tartrate tetrahydrate, [1491](#)
 Potassium sorbate, [1495](#)
 Potassium tartrate hemihydrate, [1505](#)
 Potato starch, *see* Starch, [1833](#)
 Povidone 25, soluble, [1511](#)
 Povidone iodine, [1517](#)
 Povidonum 25, solubile, *see* Povidone 25, soluble, [1511](#)
 Povidonum iodinatum, *see* Povidone iodine, [1517](#)
 Prasterone, [1523](#)
 Prasteronum, *see* Prasterone, [1523](#)
 Prednicarbate, micronized, [1529](#)
 Prednicarbatum micronisatum, *see* Prednicarbate, micronized, [1529](#)
 Prednisolon dihydrogen phosphate dinatrium, [1541](#)
 Prednisolone acetate, [1547](#)
 Prednisolone hydrogen succinate, [1559](#)
 Prednisolone, micronized, [1563](#)
 Prednisoloni acetat, *see* Prednisolone acetate, [1547](#)
 Prednisoloni hydrogensuccinas, *see* Prednisolone hydrogen succinate, [1559](#)
 Prednisoloni natrii phosphas, *see* Prednisolon dihydrogen phosphate dinatrium, [1541](#)
 Prednisolonum micronisatum, *see* Prednisolone, micronized, [1563](#)
 Prednisonum, *see* Prednisone, [1575](#)
 Pregnenolone, [1581](#)
 Pregnenolonum, *see* Pregnenolone, [1581](#)
 Prilocaine hydrochloride, [1587](#)
 Prilocaini hydrochloridum, *see* Prilocaine hydrochloride, [1587](#)
 Procaine hydrochloride, [1593](#)
 Procaini hydrochloridum, *see* Procaine hydrochloride, [1593](#)
 Progesterone, micronized, [1599](#)
 Progesteronum micronisatum, *see* Progesterone, micronized, [1599](#)
 Prolinum, *see* L-proline, [1045](#)
 Promethazine hydrochloride, [1613](#)
 Promethazini hydrochloridum, *see* Promethazine hydrochloride, [1613](#)
 Propranolol hydrochloride, [1617](#)
 Propranololi hydrochloridum, *see* Propranolol hydrochloride, [1617](#)
 Propyl-4-hydroxybenzoate, [1625](#)
 Propylis parahydroxybenzoas, *see* Propyl-4-hydroxybenzoate, [1625](#)
 Propyphenazone, [1631](#)
 Propyphenazonum, *see* Propyphenazone, [1631](#)
 Pyridoxal-5-phosphate, [1637](#)
 Pyridoxali phosphas, *see* Pyridoxal-5-phosphate, [1637](#)
 Pyridoxine hydrochloride, [1643](#)
 Pyridoxini hydrochloridum, *see* Pyridoxine hydrochloride, [1643](#)
 Quinidine sulfate, *see* Quinidine sulfate dihydrate, [1649](#)
 Quinidine sulfate dihydrate, [1649](#)
 Quinine dihydrochloride, [1653](#)
 Quinine hydrochloride, [1657](#)
 Quinine sulfate, [1663](#)
 Quinoline yellow, [1667](#)
 Quinolinol sulfate potassium sulfate, [1673](#)
 Quinolinol sulphate potassium sulphate, *see* Quinolinol sulfate potassium sulfate, [1673](#)
 Resocrinol, [1679](#)
 Resorcinolum, *see* Resocrinol, [1679](#)
 Ribavirin, [1685](#)
 Ribavirinum, *see* Ribavirin, [1685](#)
 Riboflavin, [1689](#)
 Riboflavin phosphate sodium, [1695](#)
 Riboflavinum, *see* Riboflavin, [1689](#)
 Rice starch, *see* Starch, [1833](#)
 Ropivacaine hydrochloride monohydrate, [1699](#)
 Ropivacaini hydrochloridum monohydricum, *see* Ropivacaine hydrochloride monohydrate, [1699](#)

- Saccharin sodium, [1703](#)
 Saccharinum natricum, *see* Saccharin sodium, [1703](#)
 Saccharum, *see* Sucrose, [1847](#)
 Salicylic acid, [1709](#)
 Scopolamini hydrobromidum, *see* Hyoscine hydrobromide, [917](#)
 Selenium yeast, [1723](#)
 Serine, [1727](#)
 Serinum, *see* Serine, [1727](#)
 Sildenafil citrate, [1731](#)
 Sildenafil citras, *see* Sildenafil citrate, [1731](#)
 Sodium acetate trihydrate, [1737](#)
 Sodium ascorbate, [1743](#)
 Sodium benzoate, [1749](#)
 Sodium citrate, [1757](#)
 Sodium cromoglicate, [1769](#)
 Sodium cyclamate, [1775](#)
 Sodium dodecyl sulfate, *see* Waxes / Fats, [2107](#)
 Sodium dodecyl sulphate, *see* Waxes / Fats, [2107](#)
 Sodium edetate, [1781](#)
 Sodium methyl-4-hydroxybenzoate, [1789](#)
 Sodium saccharin, *see* Saccharin sodium, [1703](#)
 Sodium salicylate, powdered, [1795](#)
 Sodium tetraborate, [1799](#)
 Softisan® 601, *see* Monostereates, [1277](#)
 Sorbic acid, [1805](#)
 Sorbitan stearate, *see* Monostereates, [1277](#)
 Sorbitani stearas, *see* Monostereates, [1277](#)
 Sorbitol, [1811](#)
 Sorbitolum, *see* Sorbitol, [1811](#)
 Soy lecithin (instant form), [1819](#)
 Spironolactone, [1825](#)
 Spironolactonum, *see* Spironolactone, [1825](#)
 Starch, [1833](#)
 Stearic acid 50, [1841](#)
 Sucrose, [1847](#)
 Sulfacetamide, [1859](#)
 Sulfacetamidum, *see* Sulfacetamide, [1859](#)
 Sulfadiazine, [1865](#)
 Sulfadiazinum, *see* Sulfadiazine, [1865](#)
 Sulfogaiacol hydrate, [1871](#)
 Sulfoguaiacolum hydricum, *see* Sulfogaiacol hydrate, [1871](#)
 SyrSpend® SF Alka, *see* Starch, [1833](#)
 SyrSpend® SF pH4, *see* Starch, [1833](#)

 Tannin, [1875](#)
 Tanninum, *see* Tannin, [1875](#)
 Tartaric acid, [1883](#)
 Taurine, [1891](#)
 Taurinum, *see* Taurine, [1891](#)
 Testosterone, [1897](#)
 Testosterone propionate, [1905](#)
 Testosteroni propionas, *see* Testosterone propionate, [1905](#)
 Testosteronum, *see* Testosterone, [1897](#)
 Tetracaine base, [1915](#)
 Tetracaine hydrochloride, [1923](#)
 Tetracaini hydrochloridum, *see* Tetracaine hydrochloride, [1923](#)
 Tetracainum, *see* Tetracaine base, [1915](#)
 Tetracycline hydrochloride, [1933](#)
 Tetracyclini hydrochloridum, *see* Tetracycline hydrochloride, [1933](#)
 Thalidomide, [1941](#)
 Thalidomidum, *see* Thalidomide, [1941](#)
 Theophylline, [1945](#)
 Theophylline-ethylenediamine hydrate, [1949](#)
 Theophyllinum, *see* Theophylline, [1945](#)
 Theophyllinum et ethylenediaminum hydricum, *see* Theophylline-ethylenediamine hydrate, [1949](#)
 Thiamine chloride hydrochloride, [1953](#)
 Thiamini hydrochloridum, *see* Thiamine chloride hydrochloride, [1953](#)
 Threoninum, *see* L-threonine, [1049](#)
 Thymol, [1959](#)
 Thymolum, *see* Thymol, [1959](#)
 Tobramycin sulfate, [1965](#)
 Tobramycin sulphate, *see* Tobramycin sulfate, [1965](#)
 Tobramycini sulfas, *see* Tobramycin sulfate, [1965](#)
 Tosylchloramide sodium, [1971](#)
 Tosylchloramidum natricum, *see* Tosylchloramide sodium, [1971](#)
 Tranexamic acid, [1977](#)
 Tretinoin, [1983](#)
 Tretinoinum, *see* Tretinoin, [1983](#)
 Triamcinolone acetone, [1993](#)
 Triamcinolone, micronized, [2013](#)
 Triamcinoloni acetone, *see* Triamcinolone acetone, [1993](#)
 Triamcinolonum micronisatum, *see* Triamcinolone, micronized, [2013](#)
 Triclosan, [2019](#)
 Triclosanum, *see* Triclosan, [2019](#)
 Trometamol, [2039](#)
 Trometamolum, *see* Trometamol, [2039](#)
 Tropicamide, [2049](#)
 Tropicamidum, *see* Tropicamide, [2049](#)
 Tryptophanum, *see* L-tryptophan, [1053](#)
 Tyrosine, [2053](#)
 Tyrosinum, *see* Tyrosine, [2053](#)
 Tyrothricin, [2057](#)
 Tyrothricinum, *see* Tyrothricin, [2057](#)

 Ubidecarenone, [2063](#)
 Ubidecarenonum, *see* Ubidecarenone, [2063](#)

Urea, [2069](#)
Uridine, [2085](#)
Uridinum, *see* Uridine, [2085](#)

Valine, [2091](#)
Valinum, *see* Valine, [2091](#)
Vancomycin hydrochloride, [2095](#)
Vancomycini hydrochloridum, *see*
 Vancomycin hydrochloride, [2095](#)
Vanillin, [2101](#)
Vanillinum, *see* Vanillin, [2101](#)

Wax, bleached, *see* Waxes / Fats, [2107](#)
Wax, yellow, *see* Waxes / Fats, [2107](#)
Waxes / Fats, [2107](#)
Wheat starch, *see* Starch, [1833](#)

Wool alcohols, [2129](#)

Xylitol, [2135](#)
Xylitolum, *see* Xylitol, [2135](#)
Xylometazoline hydrochloride, [2141](#)
Xylometazolini hydrochloridum, *see*
 Xylometazoline hydrochloride, [2141](#)
Xylose, [2147](#)
Xylosum, *see* Xylose, [2147](#)

Zinc acetate dihydrate, [2153](#)
Zinc gluconate, [2159](#)
Zincum aceticum purum, *see* Zinc acetate
 dihydrate, [2153](#)
Zincum gluconicum, *see* Zinc gluconate, [2159](#)