Validation documentation
APIs & excipients, liquid/semi-solid (other)

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Validation documentation of the chemometrics database of the near-infrared spectrometer *Apo-Ident*.
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Contents

Introduction

The unequivocal proof of the identity of pharmaceutical raw materials based on a monograph or traditional alternative methods is work-intense, time-intense 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 transflection.
- 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, liquid/semi-solid (other)*.

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, liquid/semi-solid (other)*. 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. Bezugsquellennachweis 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) *Unterschrittener 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.

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, liquid/semi-solid (other)* 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 themself 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 Pharmacopeia* 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

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

[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 $\mathbf{X}$.

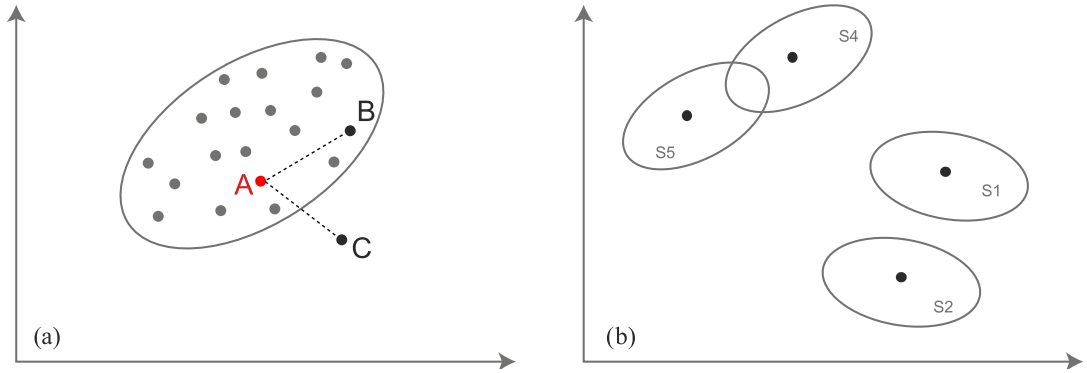

Figure 1: (a) The *Mahalanobis distance* from A to B is less than from A to C. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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 53 906 spectra from 4382 different batches for a total of 209 substances were used to validate the substance class *APIs & excipients, liquid/semi-solid (other)*.

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, liquid/semi-solid (other)	161	507	24 505

From category *A* a total of 24 505 spectra from 507 batches for a total of 161 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, liquid/semi-solid (other)	204	447	20 801

From category *B* a total of 20 801 spectra from 447 batches for a total of 204 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, liquid/semi-solid (other)	150	3611	8600

From category *C* a total of 8600 spectra from 3611 batches for a total of 150 substances were taken into account for validation.

Validation results

The validation runs checked whether all substances/substance groups in the substance class *APIs & excipients, liquid/semi-solid (other)* 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, liquid/semi-solid (other)* 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	24 505	0	2 401 490
Type B	0	16 295	1096	2 040 748
Type C	0	8110	345	842 906

All substances/substance groups in the substance class *APIs & excipients, liquid/semi-solid (other)* 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 60 %)	100.000 00 % (> 99.960 67 %)
Typ B	100.000 00 % (> 99.999 45 %)	92.093 30 % (> 92.061 49 %)
Typ C	100.000 00 % (> 99.987 87 %)	93.849 95 % (> 93.187 07 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 2.3-2021-01

Validated substance/substance group	**Alfason Basis Cresa®**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30723-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Alfason Basis Cresa®

Special notes

When selecting the *Alfason Basis Cresa®* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Alfason Basis Cresa®	4	1	41

Second-stage model

For differentiation of the substance/substance group *Alfason Basis Cresa*® the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Alfason Basis Cresa*®:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Astellas Pharma	Alfason Basis Cr…	12B11/77	30723	54	not required
Astellas Pharma	Alfason Basis Cr…	13D06/75	31071	40	not required
Astellas Pharma	Alfason Basis Cr…	15I46/79	32064	60	not required
Astellas Pharma	Alfason Basis Cr…	16D35/77	32815	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 194 spectra of 4 reference samples from the substance/substance group *Alfason Basis Cresa*®. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.

- 24 311 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Alfason Basis Cresa*®.

- 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
LEO Pharma GmbH	Alfason Basis Cresa®	17B27/75	33487	40
Astellas Pharma	Alfason Basis Cresa®	16D35/77	32840	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 20 *Apo-Ident* customers from 42 batches from the substance/substance group *Alfason Basis Cresa®*.

- Among them are spectra of independent samples from 41 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.	Alfason Basis Cresa®	12/05/75	1
AHD	Alfason Basis Cresa®	13A18/76	1
Alfason/Gehe	Alfason Basis Cresa®	161J31/75	1
Alfason/krieger	Alfason Basis Cresa®	17F10/76	1
anzag	Alfason Basis Cresa®	18I13/76	2
Astellas	Alfason Basis Cresa®	13A16/76	1
Astellas	Alfason Basis Cresa®	14J02/77	1
Astellas	Alfason Basis Cresa®	14c32-78	1
AStellas	Alfason Basis Cresa®	14J02/77	1
Astellas / Anzag	Alfason Basis Cresa®	15J3/79	1
Astellas / Noweda	Alfason Basis Cresa®	14J02/77	1
Astellas / Noweda	Alfason Basis Cresa®	15D11/79	2
Astellas / Noweda	Alfason Basis Cresa®	15D1179	1
Astellas / Noweda	Alfason Basis Cresa®	15J35/76	1
Astellas Pharma	Alfason Basis Cresa®	13K15/75	2
Astellas Pharma	Alfason Basis Cresa®	14C32/78	1
Astellas Pharma	Alfason Basis Cresa®	14J02/77	2
Astellas Pharma	Alfason Basis Cresa®	15D11/79	3
Astellas Pharma	Alfason Basis Cresa®	16A06/76	1
Astellas Pharma	Alfason Basis Cresa®	15H06/80	1
Astellas Pharma GmbH	Alfason Basis Cresa®	16H03/76	1
Astellas Pharma GmbH/ A...	Alfason Basis Cresa®	16D35/77	1
Astellas Pharma/Noweda	Alfason Basis Cresa®	15J38/79	1
Astellas/Alliance	Alfason Basis Cresa®	15H06/80	1
Astellas/Alliance	Alfason Basis Cresa®	15J35/75	1
Astellas/Alliance	Alfason Basis Cresa®	16J31/75	1
Astellas/Gehe	Alfason Basis Cresa®	14C32/78	1
Astellas/Gehe	Alfason Basis Cresa®	15B14/76	1
Astellas/Gehe	Alfason Basis Cresa®	16G03/75	1
Caelo	Alfason Basis Cresa®	15J35/75	1
Caelo	Alfason Basis Cresa®	17EB/75	1
Caelo	Alfason Basis Cresa®	17EB2/75	1
Caelo	Alfason Basis Cresa®	17017/76	1
Caeo/Noweda	Alfason Basis Cresa®	15H06/80	1
devesa/Phönix	Alfason Basis Cresa®	17F08/76	2
Ichtyol/Phönix	Alfason Basis Cresa®	13E08/75	1
Lamotte/ Noweda	Alfason Basis Cresa®	16A06/76	2
Leo Pharma	Alfason Basis Cresa®	19D65/76	1
LEO Pharma / Alliance H...	Alfason Basis Cresa®	17F20/76	1
LEO Pharma / Noweda	Alfason Basis Cresa®	17EB2/75	2
LEO Pharma / Noweda	Alfason Basis Cresa®	18D20/75(3x350g)	1

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Supplier	Substance	Batch	Spectra
Leo Pharma/Gehe	Alfason Basis Cresa®	18A29/75	1
LEO Pharma/Gehe	Alfason Basis Cresa®	19D87/75	1
Leo Pharma/Phönix	Alfason Basis Cresa®	19D87/75	1
Leo/ Phönix	Alfason Basis Cresa®	17F46/76	2
Leo/Alliance	Alfason Basis Cresa®	18D20/75	2
LEO/Alliance Healthcare	Alfason Basis Cresa®	18D19/76	1
Leo/Gehe	Alfason Basis Cresa®	17C17/76	1
Leo/Gehe	Alfason Basis Cresa®	17F44/76	1
Leo/Gehe	Alfason Basis Cresa®	18J36/75	1
Leo/Phönix	Alfason Basis Cresa®	18A29/75	1
Leopharm/AEP	Alfason Basis Cresa®	17EB3/75	2
Leopharm/Alliance hc	Alfason Basis Cresa®	18D20/75	2
Noweda-Astella	Alfason Basis Cresa®	15A01/79	1
Sanacorp	Alfason Basis Cresa®	12F23/76	1
Sanacorp	Alfason Basis Cresa®	13A16/76	1
Sanacorp	Alfason Basis Cresa®	13E08/75	1

- 8530 spectra from 734 *Apo-Ident* customers from a total of 3504 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	194	0	24 311
Type B	0	80	0	20 721
Type C	0	69	1	8530

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.9072 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7857 %)	98.5714 % (> 94.2857 %)

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 *Alfason Basis Cresa®* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Alfason® Repair	14.29	–
Linola® H fat N	17.37	–
Linola® fat cream	18.00	–
Neribas® ointment	25.69	–
Asche Basis® ointment	33.46	–
Dermatop® base ointment	35.76	–
Bepanthen® Wund- und Heilsalbe	40.45	–
Excipial® lipo cream	76.05	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32064	32064	0.00	24.03
31071	31071	0.00	18.97
32815	32815	0.00	17.26
30723	30723	0.00	20.44

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 2.3-2021-01

Validated substance/substance group	**Allergika evening primrose oil cream 20% / Dermifant® kids cr**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30970-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Allergika evening primrose oil cream 20% / Dermifant® kids cream; Allergika evening primrose oil cream 20%; Dermifant® kids cream

Special notes

When selecting the *Allergika evening primrose oil cream 20% / Dermifant® kids cream* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Allergika evening primrose oil cream 20%	3	2	0
Dermifant® kids cream	3	2	10

Second-stage model

For differentiation of the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Allergika	Allergika evenin…	1504021	31725	60	not required
Allergika	Allergika evenin…	1511051	31871	60	not required
Allergika	Allergika evenin…	1609043	33486	40	not required
Allergika	Dermifant® kids …	1210082	30970	80	not required
Allergika	Dermifant® kids …	1303033	31062	40	not required
Allergika	Dermifant® kids …	1705043	33639	40	not required

Validation samples

A total of 53 906 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 *Allergika evening primrose oil cream 20% / Dermifant® kids cream*. These samples are listed above in the *calibration samples* section. The reference samples come from 6 different batches.

- 24 185 spectra from a total of 498 batches from further 159 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Allergika evening primrose oil cream 20% / Dermifant® kids cream*.

- 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
Allergika	Allergika evening primrose o...	1607031	32756	40
Allergika	Allergika evening primrose o...	1410062	32909	40
Allergika	Dermifant® kids cream	1607032	32754	40
Allergika	Dermifant® kids cream	1801010	34033	40

- 20 641 spectra from a total of 443 batches from further 202 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 11 batches from the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream*.

- 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
Allergika Pharma GmbH	Dermifant® kids cream	1410072	1
Allergika Pharma/Alliance	Dermifant® kids cream	1511052	1
Allergika/Gehe	Dermifant® kids cream	1502013	1
Allergika/Phönix	Dermifant® kids cream	1509042	1
Gehe	Dermifant® kids cream	1407053	1
Phönix	Dermifant® kids cream	1312102	2
Phönix EK:10,19 EUR ...	Dermifant® kids cream	1703024	1
Sanacorp WE: 01.09.17 ...	Dermifant® kids cream	1705043	1
Sanacorp WE: 09.11.17 1...	Dermifant® kids cream	1708063	2
Sanacorp7Mida WE:13.01...	Dermifant® kids cream	1711094	4
WE:Phoenix 10.12.2016 ...	Dermifant® kids cream	1609042	1

- 8584 spectra from 736 *Apo-Ident* customers from a total of 3535 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Allergika evening primrose oil cream 20% / Dermifant® kids cream* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 185
Type B	0	160	0	20 641
Type C	0	16	0	8584

The substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.7888 %)	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 *Allergika evening primrose oil cream 20% / Dermifant® kids cream* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Excipial® U Lipolotio	13.60	–
Lipoderm® lotion	21.47	–
DMS® base cream high classic	21.64	–
Dermatest base ointment	22.43	–
Lipolotio urea 5% F body lotion	23.70	–
DMS® base cream high classic plus	26.68	–
Abitima® clinic body cream	30.47	–
Neuroderm® moisturising cream lipo	36.76	–
Excipial® U10 Lipolotio	39.14	–
Eucerinum W/O basis	42.79	–
Neuroderm® moisturising cream	43.80	–
DMS® base cream classic	48.00	–
Hans Karrer Lipocream MicroSilver	49.53	–
Fabitop® base cream	62.31	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Allergika evening primrose oil cream 20% / Dermifant® kids cream* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30970	30970	0.00	17.59
31062	31062	0.00	21.25
33639	33639	0.00	18.50
31725	31725	0.00	19.28
31871	31871	0.00	17.74
33486	33486	0.00	18.08

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 2.3-2021-01

Validated substance/substance group	**alpha-bisabolol (racemic) at least 85%**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31464-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

alpha-bisabolol (racemic) at least 85%

Special notes

When selecting the *alpha-bisabolol (racemic) at least 85%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

A sample is considered independent 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-bisabolol (racemic) at least 85%	1	3	7

Second-stage model

For differentiation of the substance/substance group *alpha-bisabolol (racemic) at least 85%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan 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-bisabolol (racemic) at least 85%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	alpha-bisabolol …	13360114	31464	60	not required
Caelo	alpha-bisabolol …	13360114	31465	60	not required

Validation samples

A total of 53 906 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 *alpha-bisabolol (racemic) at least 85%*. These samples are listed above in the *calibration samples* section. The reference samples come from 1 different batches.

- 24 385 spectra from a total of 503 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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-bisabolol (racemic) at least 85%*.

- 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	alpha-bisabolol (racemic) at…	16271902	32782	40
Caelo	alpha-bisabolol (racemic) at…	17065801	33417	40
Caelo	alpha-bisabolol (racemic) at…	180585	34227	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 batches from the substance/substance group *alpha-bisabolol (racemic) at least 85%*.

- 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	alpha-bisabolol (racemic) at…	14322713	1
Caelo	alpha-bisabolol (racemic) at…	18058503	1
Caelo	alpha-bisabolol (racemic) at…	18306002	1
Caelo	alpha-bisabolol (racemic) at…	18306001	2
Caelo	alpha-bisabolol (racemic) at…	18058504	1
Caelo	alpha-bisabolol (racemic) at…	18058506	1
Spangro 28.01.2019	alpha-bisabolol (racemic) at…	18058506	1
Spangro 28.1.2019	alpha-bisabolol (racemic) at…	180580506	1

- 8591 spectra from 736 *Apo-Ident* customers from a total of 3539 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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-bisabolol (racemic) at least 85%* can clearly be 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-bisabolol (racemic) at least 85%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	120	0	20 681
Type C	0	9	0	8591

The substance/substance group *alpha-bisabolol (racemic) at least 85%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7920 %)	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 *alpha-bisabolol (racemic) at least 85%* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citronella oil	49.66	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *alpha-bisabolol (racemic) at least 85%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31464	31464	0.00	51.41
31465	31465	0.00	51.19

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 2.3-2021-01

Validated substance/substance group	**Angelica root oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30535-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Angelica root oil; Oleum angelicae (e radice)

Special notes

When selecting the *Angelica root oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Angelica root oil	5	2	7

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Angelica root oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Angelica root oil	33019-109871BAG90451	30964	40	not required
Taoasis	Angelica root oil	4053-116078	31682	60	not required
Taoasis	Angelica root oil	2829199-122587	31780	60	not required
Taoasis	Angelica root oil	3029209-123992	32068	60	not required
Taoasis	Angelica root oil	B3039-9598	35074	20	not required

Validation samples

A total of 53 906 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 *Angelica root oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.
- 24 265 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 3 reference samples from the substance/substance group *Angelica root oil*.
- 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
Taoasis	Angelica root oil	3029209-125059	32477	40
Taoasis	Angelica root oil	1839219-127663	33644	40
Taoasis	Angelica root oil	B3039-9598	35074†	20

- 20 701 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 4 *Apo-Ident* customers from 7 batches from the substance/substance group *Angelica root oil*.

- 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	Angelica root oil	11352706	1
Taoasis	Angelica root oil	33019-110236BAG904	1
Taoasis	Angelica root oil	4053-117762	1
Taoasis	Angelica root oil	3629209-126289	1
Taoasis	Angelica root oil	1049239-3525	1
Taoasis	Angelica root oil	32229229-1384	1
Taoasis	Angelica root oil	129271	1

- 8593 spectra from 736 *Apo-Ident* customers from a total of 3539 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Angelica root oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Angelica root oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 265
Type B	0	80	20	20 701
Type C	0	6	1	8593

†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 *Angelica root oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9455 %)	80.0000 % (> 77.0000 %)
Type C	100.0000 % (> 98.7941 %)	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 *Angelica root oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dwarf pine oil	14.35	–
Spearmint oil	24.88	–
Frankincense oil	26.71	–
Swiss pine oil	29.87	–
Marjoram oil	31.61	–
Silver fir oil	38.30	–
Spruce needle oil	38.86	–
Citus oil	41.57	–
Juniper oil	42.63	–
Cumin oil	44.49	–
Camphor oil	44.55	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
35074	35074	0.00	16.64
31780	31780	0.00	31.73
32068	32068	0.00	26.91

continued on the next page

continued from previous page

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31682	31682	0.00	26.71
30964	30964	0.00	30.38

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 2.3-2021-01

Validated substance/substance group	**Anise oil, organic**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30670-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Anise oil, organic; Oleum Anisi stellati

Special notes

When selecting the *Anise oil, organic* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Anise oil, organic	2	3	26

Second-stage model

For differentiation of the substance/substance group *Anise oil, organic* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Anise oil, organic*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Anise oil, organic	2241027-120475	31681	60	not required
Taoasis	Anise oil, organic	1492-125379	32794	40	not required
Taoasis	Anise oil, organic	1492-125379	32935	40	not required

Validation samples

A total of 53 906 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 *Anise oil, organic*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 365 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Anise oil, organic*.
- 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
Taoasis	Anise oil, organic	B080009-99431BAG90451	30670	40
Taoasis	Anise oil, organic	42803-290	33622	40
Taoasis	Anise oil, organic	42803-3438	34288	40
Taoasis	Anise oil, organic	42803-290	33875	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 33 spectra from 17 *Apo-Ident* customers from 28 batches from the substance/substance group *Anise oil, organic*.

- 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
Caelo	Anise oil, organic	12322503	1
Caelo	Anise oil, organic	15148901	1
Caelo	Anise oil, organic	18307513	1
Caelo	Anise oil, organic	13056105	1
Caelo	Anise oil, organic	12322507	1
Caelo	Anise oil, organic	17150001	1
Phönix 10.04.2017	Anise oil, organic	15337020	1
Schubert	Anise oil, organic	1236E0-1518	1
Taoasis	Anise oil, organic	26735-110455	1
Taoasis	Anise oil, organic	26735-108555	1
Taoasis	Anise oil, organic	26735-111137	2
Taoasis	Anise oil, organic	26735-113054	1
Taoasis	Anise oil, organic	130910-113040	1
Taoasis	Anise oil, organic	26569-115911	2
Taoasis	Anise oil, organic	2241027-120196	1
Taoasis	Anise oil, organic	1492-121627	1
Taoasis	Anise oil, organic	1492-123225	1
Taoasis	Anise oil, organic	1492-125315	1
Taoasis	Anise oil, organic	42803-127333	1
Taoasis	Anise oil, organic	42803-290	1
Taoasis	Anise oil, organic	42803-1177	1
Taoasis	Anise oil, organic	42803-772	1
Taoasis	Anise oil, organic	2336-5388	1
Taoasis/Noweda	Anise oil, organic	1465-121083h08	1
Taoasis/Noweda	Anise oil, organic	2241027-120928H07	1
Taoasis/Sanacorp	Anise oil, organic	26735-112250	1
Taoasis/Sanacorp	Anise oil, organic	26735-111137	2
Apotheker S Bauer&Comp	Anise oil, organic		1
Taoasis	Anise oil, organic	1492-125379	2

- 8567 spectra from 734 *Apo-Ident* customers from a total of 3518 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Anise oil, organic* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Anise oil, organic* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	134	26	20 601
Type C	0	29	4	8567

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9458 %)	83.7500 % (> 81.8750 %)
Type C	100.0000 % (> 98.7867 %)	87.8788 % (> 78.7879 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Fennel oil	44.48	–
Basil oil	84.08	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31681	31681	0.00	44.48
32794	32794	0.00	46.44
32935	32935	0.00	49.62

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 2.3-2021-01

Validated substance/substance group	**Argan oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	32168-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Argan oil; Oleum Arganiae

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Argan oil	2	2	3

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Argan oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Argan oil	161443	32168	60	-*
Caelo	Argan oil	16035101	32571	40	not required

Validation samples

A total of 53 906 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 *Argan oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 405 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Argan oil*.
- 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	Argan oil	162759	32679	40
Caelo	Argan oil	190980	34461	40
Caelo	Argan oil	16035101	32306	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Argan oil*.

- 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	Argan oil	17198305	1
Caesar & Loretz GmbH	Argan oil	19116406	1
Caesar & Loretz GmbH	Argan oil	18122701	1

- 8597 spectra from 736 *Apo-Ident* customers from a total of 3543 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Argan oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Argan oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 405
Type B	0	120	0	20 681
Type C	0	3	0	8597

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8065 %)	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 *Argan oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Balm Bio Nature	10.72	–
Excipial® almond oil ointment	24.75	–
Wax ointment (stabilised)	59.13	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32168	32168	0.00	17.84
32571	32571	0.00	14.41

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 2.3-2021-01

Validated substance/substance group	**Balm Bio Nature**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31645-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Balm Bio Nature

Special notes

When selecting the *Balm Bio Nature* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Balm Bio Nature	3	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Balm Bio Nature*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Balm Bio Nature	150422-5106	31645	60	not required
Taoasis	Balm Bio Nature	150422-5106	31724	60	not required
Taoasis	Balm Bio Nature	151210-5337	32994	40	not required
Taoasis	Balm Bio Nature	180515-8060	34115	40	not required

Validation samples

A total of 53 906 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 *Balm Bio Nature*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.

- 24 305 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Balm Bio Nature*.

- 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
Taoasis	Balm Bio Nature	160401-6083	32786	40
Taoasis	Balm Bio Nature	170403-7087	33436	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 1 batches from the substance/substance group *Balm Bio Nature*.

- 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
Taoasis	Balm Bio Nature	151210-5337	12

- 8588 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Balm Bio Nature* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Balm Bio Nature* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	80	0	20 721
Type C	0	12	0	8588

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7902 %)	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 *Balm Bio Nature* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Excipial® almond oil ointment	10.80	–
Argan oil	14.03	–
Wax ointment (stabilised)	43.08	–
Salicylic white paraffin 10%	52.22	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31645	31645	0.00	16.03
31724	31724	0.00	19.98
32994	32994	0.00	10.80
34115	34115	0.00	19.73

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 2.3-2021-01

Validated substance/substance group	**Banana aroma**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31105-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Banana aroma; Banana flavour

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Banana aroma	3	1	11

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Banana aroma*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Banana aroma	12302509	31105	40	1404166
Caelo	Banana aroma	14353702	31606	60	not required
Caelo	Banana aroma	171890	33687	40	20170707*

Validation samples

A total of 53 906 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 *Banana aroma*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Banana aroma*.
- 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	Banana aroma	16089305	33496	40
Caelo	Banana aroma	16089305	33608	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 15 *Apo-Ident* customers from 12 batches from the substance/substance group *Banana aroma*.

- 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	Banana aroma	14353707	1
Caelo	Banana aroma	16089304	2
Caelo	Banana aroma	14353709	1
Caelo	Banana aroma	17189002	2
Caelo	Banana aroma	17189001	3
Caelo	Banana aroma	18017202	1
Caelo	Banana aroma	19185301	1
Caelo	Banana aroma	16089305	1
Caelo	Banana aroma	18017201	1
Caelo	Banana aroma	191853001	1
Caelo	Banana aroma	18017205	1
Caesar & Loretz GmbH	Banana aroma	18017202	1
Caesar & Loretz GmbH	Banana aroma	18017205	1
Caesar & Loretz GmbH/Sa…	Banana aroma	19185301	1
Caelo	Banana aroma	12302509	1

- 8581 spectra from 736 *Apo-Ident* customers from a total of 3534 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Banana aroma* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Banana aroma* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	19	0	8581

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7882 %)	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 *Banana aroma* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Nicotine	115.93	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31105	31105	0.00	173.33
31606	31606	0.00	172.54
33687	33687	0.00	171.22

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 2.3-2021-01

Validated substance/substance group	**Basil oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30751-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Basil oil; Oleum ocimum basilicum

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Basil oil	2	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Basil oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Basil oil	561-119057	31755	60	not required
Taoasis	Basil oil	1500312-128851	33725	40	not required

Validation samples

A total of 53 906 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 *Basil oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 405 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Basil oil*.
- 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
Taoasis	Basil oil	21022-108746BAG90451	30751	40
Taoasis	Basil oil	1500312-126393	32972	40
Taoasis	Basil oil	1500312-126393	32973	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Basil oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Basil oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Basil oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 405
Type B	0	120	0	20 681
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Basil oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Anise oil, organic	88.75	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31755	31755	0.00	153.82
33725	33725	0.00	159.65

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 2.3-2021-01

Validated substance/substance group	**Benzoin siam oil 20%**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30456-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Benzoin siam oil 20%; Oleum styrax tonkinensis

Special notes

When selecting the *Benzoin siam oil 20%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Benzoin siam oil 20%	5	1	13

Second-stage model

For differentiation of the substance/substance group *Benzoin siam oil 20%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Benzoin siam oil 20%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Benzoin siam oil…	12990-114892	31256	40	not required
Taoasis	Benzoin siam oil…	51939-123084	31843	60	not required
Taoasis	Benzoin siam oil…	63287-126233	32974	40	not required
Taoasis	Benzoin siam oil…	2161-1395	33855	40	not required
Taoasis	Benzoin siam oil…	32105-119788BAG90451	33944	40	not required

Validation samples

A total of 53 906 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 *Benzoin siam oil 20%*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.

- 24 285 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Benzoin siam oil 20%*.

- 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
Taoasis	Benzoin siam oil 20%	2010-836	33724	40
Taoasis	Benzoin siam oil 20%	63287-126233	33028	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 15 batches from the substance/substance group *Benzoin siam oil 20%*.

- 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
Taoasis	Benzoin siam oil 20%	518434-108321	1
Taoasis	Benzoin siam oil 20%	541389-111081	1
Taoasis	Benzoin siam oil 20%	548442-113119	1
Taoasis	Benzoin siam oil 20%	548481-111780	1
Taoasis	Benzoin siam oil 20%	23478-116955	2
Taoasis	Benzoin siam oil 20%	31343-118365	1
Taoasis	Benzoin siam oil 20%	41242-120661	1
Taoasis	Benzoin siam oil 20%	41242-121512	1
Taoasis	Benzoin siam oil 20%	54125	1
Taoasis	Benzoin siam oil 20%	59023-125420	1
Taoasis	Benzoin siam oil 20%	62330-124547	1
Taoasis	Benzoin siam oil 20%	17578-116819	1
Taosis	Benzoin siam oil 20%	474084-96350	1
Taoasis	Benzoin siam oil 20%	51939-123084	1
Taoasis	Benzoin siam oil 20%	63287-126233	1

- 8584 spectra from 736 *Apo-Ident* customers from a total of 3531 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Benzoin siam oil 20%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Benzoin siam oil 20%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 285
Type B	0	67	13	20 721
Type C	0	15	1	8584

The substance/substance group *Benzoin siam oil 20%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9456 %)	83.7500 % (> 80.0000 %)
Type C	100.0000 % (> 98.7888 %)	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 *Benzoin siam oil 20%* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Oregano oil	91.26	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Benzoin siam oil 20%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33855	33855	0.00	98.66
31843	31843	0.00	91.26
32974	32974	0.00	96.40
33944	33944	0.00	100.85
31256	31256	0.00	91.58

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 2.3-2021-01

Validated substance/substance group	**Bepanthen® Wund- und Heilsalbe**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31048-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Bepanthen® Wund- und Heilsalbe

Special notes

When selecting the *Bepanthen® Wund- und Heilsalbe* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bepanthen® Wund- und Heilsalbe	3	2	2

Second-stage model

For differentiation of the substance/substance group *Bepanthen® Wund- und Heilsalbe* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Bepanthen® Wund- und Heilsalbe*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bayer	Bepanthen® Wund-…	GP00LB9	31048	40	not required
Bayer	Bepanthen® Wund-…	GP012SS	31758	60	not required
Bayer	Bepanthen® Wund-…	GP01CTH	33613	40	not required

Validation samples

A total of 53 906 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 *Bepanthen® Wund- und Heilsalbe*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Bepanthen® Wund- und Heilsalbe*.
- 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
Bayer	Bepanthen® Wund- und Heilsalbe	GP018T5	32720	40
Bayer	Bepanthen® Wund- und Heilsalbe	GP019ZF	32948	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Bepanthen® Wund- und Heilsalbe*.

- 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
Bayer	Bepanthen® Wund- und Heilsalbe	GP01AUE	1
Bombastus	Bepanthen® Wund- und Heilsalbe	GP01-DR9	1

- 8598 spectra from 736 *Apo-Ident* customers from a total of 3544 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Bepanthen® Wund- und Heilsalbe* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bepanthen® Wund- und Heilsalbe* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	2	0	8598

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8173 %)	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 *Bepanthen® Wund- und Heilsalbe* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Asche Basis® ointment	14.14	–
Neribas® ointment	19.78	–
Alfason Basis Cresa®	35.65	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31048	31048	0.00	31.48
31758	31758	0.00	34.63
33613	33613	0.00	34.89

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 2.3-2021-01

Validated substance/substance group	**Bergamot oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30307-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Bergamot oil; Oleum citrus bergamia

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Bergamot oil	2	2	18

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Bergamot oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bombastus	Bergamot oil	290998	31641	60	not required
Bombastus	Bergamot oil	290998	31760	60	not required
Taoasis	Bergamot oil	3221028-121642	31784	60	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 3 reference samples from the substance/substance group *Bergamot oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 325 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Bergamot oil*.
- 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
Primavera	Bergamot oil	00189A27	34387	40
Taoasis	Bergamot oil	1968-128263	33437	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 15 *Apo-Ident* customers from 18 batches from the substance/substance group *Bergamot oil*.
- 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	Bergamot oil	264008	1
Bombastus	Bergamot oil	280260	1
Bombastus	Bergamot oil	53731-125890	1
Bombastus	Bergamot oil	19006566	1
Caelo	Bergamot oil	12020702	1
Caelo	Bergamot oil	13141501	2
Kaders	Bergamot oil	130564	1
Noweda	Bergamot oil	271858	1
Caelo	Bergamot oil	7962	1
Taoasis	Bergamot oil	32338-109135	1
Taoasis	Bergamot oil	B130301-110610	1
Taoasis	Bergamot oil	96243	1
Taoasis	Bergamot oil	33110-110701	1
Taoasis	Bergamot oil	32579-111866	1
Taoasis	Bergamot oil	33697-112408	1
Taoasis	Bergamot oil	d01be14m-121110bag90	1
Taoasis	Bergamot oil	73340-506	1
Taoasis	Bergamot oil	77879-3984	1

- 8581 spectra from 735 *Apo-Ident* customers from a total of 3528 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Bergamot oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Bergamot oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	15	4	8581

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7882 %)	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 *Bergamot oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Chamomile (essential oil)	24.75	–
Spearmint oil	36.24	–
Dwarf pine oil	55.71	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31784	31784	0.00	28.88
31641	31641	0.00	32.30
31760	31760	0.00	30.56

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 2.3-2021-01

Validated substance/substance group	**Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30966-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil; Cajeput (essentiel oil); Eucalyptus oil; Niaouli oil; Oleum Cajeputi artificiale; Oleum eucalypti; Oleum niaouli; Oleum rosmarini; Rosemary oil

Special notes

When selecting the *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cajeput (essentiel oil)	4	1	29
Eucalyptus oil	4	4	46
Niaouli oil	5	1	9
Rosemary oil	4	1	19

Second-stage model

For differentiation of the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Cajeput (essenti…	00012A27	34401	40	not required
Taoasis	Cajeput (essenti…	130829-112094BAG90451	31136	40	not required
Taoasis	Cajeput (essenti…	1662-124326	32173	40	not required
Taoasis	Cajeput (essenti…	1724-127033	33657	40	not required
Primavera	Eucalyptus oil	00178A27	34374	40	not required
Taoasis	Eucalyptus oil	527885-109705A	30966	40	not required
Taoasis	Eucalyptus oil	7271001-121014	31694	60	not required
Taoasis	Eucalyptus oil	043127A-125381	32903	40	not required
Caelo	Niaouli oil	13099606	31420	60	AR-14-FG-012561-01
Primavera	Niaouli oil	00410K26	34380	40	not required
Taoasis	Niaouli oil	34167-116962	31548	60	not required
Taoasis	Niaouli oil	40428-124242	32174	40	not required
Taoasis	Niaouli oil	1500450-125771	32970	40	not required
Taoasis	Rosemary oil	3231031-117639	31551	60	not required
Taoasis	Rosemary oil	1921019-120666	31691	60	not required
Taoasis	Rosemary oil	1862-126630	32933	40	not required
Taoasis	Rosemary oil	2150-2819	34104	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 780 spectra of 17 reference samples from the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 17 different batches.
- 23 725 spectra from a total of 487 batches from further 157 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil*.
- 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
Taoasis	Cajeput (essentiel oil)	2216-2921	34114	40
Primavera	Eucalyptus oil	00650K25	33808	40
Primavera	Eucalyptus oil	00256A26	33955	40
Primavera	Eucalyptus oil	00710C26	34172	40
Taoasis	Eucalyptus oil	41192-129138	33621	40
Taoasis	Niaouli oil	1500450-1985	34040	40
Taoasis	Rosemary oil	1614-125089	32802	40
Taoasis	Cajeput (essentiel oil)	1724-127033	33022	40
Taoasis	Cajeput (essentiel oil)	1724-127033	33023	40
Taoasis	Niaouli oil	1500450-125771	32971	40

- 20 401 spectra from a total of 438 batches from further 200 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 146 spectra from 58 *Apo-Ident* customers from 105 batches from the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil*.
- Among them are spectra of independent samples from 103 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Aurica	Cajeput (essentiel oil)	11024710	1
Bombastus	Cajeput (essentiel oil)	18001011	1
PVL	Cajeput (essentiel oil)	150712	1
Taoasis	Cajeput (essentiel oil)	24077-106468	1
Taoasis	Cajeput (essentiel oil)	L201323018-113057	1
Taoasis	Cajeput (essentiel oil)	130829-113045	1
Taoasis	Cajeput (essentiel oil)	131010-117241	2
Taoasis	Cajeput (essentiel oil)	131010-115487	2
Taoasis	Cajeput (essentiel oil)	661027-117257	2
Taoasis	Cajeput (essentiel oil)	131010-117257	1
Taoasis	Cajeput (essentiel oil)	6781012-119058	1
Taoasis	Cajeput (essentiel oil)	661027-118368	1
Taoasis	Cajeput (essentiel oil)	1301-121889	1
Taoasis	Cajeput (essentiel oil)	1518-122691	1
Taoasis	Cajeput (essentiel oil)	1518-122790	1

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Supplier	Substance	Batch	Spectra
Taoasis	Cajeput (essentiel oil)	1662-124870	1
Taoasis	Cajeput (essentiel oil)	1724-125910	1
Taoasis	Cajeput (essentiel oil)	1724-127010	2
Taoasis	Cajeput (essentiel oil)	1724-126425	1
Taoasis	Cajeput (essentiel oil)	1724-127654	1
Taoasis	Cajeput (essentiel oil)	1724-129091	1
Taoasis	Cajeput (essentiel oil)	1989-955	3
Taoasis	Cajeput (essentiel oil)	1989-1032	2
Taoasis	Cajeput (essentiel oil)	1989-956	1
Taoasis	Cajeput (essentiel oil)	2490-5372	2
Taoasis	Cajeput (essentiel oil)	2490-4102	2
Taoasis	Cajeput (essentiel oil)	2490-6100	1
Taoasis	Cajeput (essentiel oil)	1301-32758	1
TAOASIS GmbH D-32758 De…	Cajeput (essentiel oil)	1989-2818	1
Taoasis/Sanacorp	Cajeput (essentiel oil)	L201323018-113057	1
Bergland	Eucalyptus oil	K801202	2
Bombastus	Eucalyptus oil	289701	1
Bombastus	Eucalyptus oil	297737	1
Bombastus	Eucalyptus oil	303336	1
Bombastus	Eucalyptus oil	305628	1
Bombastus	Eucalyptus oil	18006426	1
Bombastus	Eucalyptus oil	19002892	1
Bombastus	Eucalyptus oil	19004174	1
Bombastus	Eucalyptus oil	303327	1
Bombastus	Eucalyptus oil	19005837	1
Bombastus	Eucalyptus oil	18005784	1
Bombastus	Eucalyptus oil	307667	1
Caelo	Eucalyptus oil	11324112	1
Caelo	Eucalyptus oil	13106407LOT	1
Caelo	Eucalyptus oil	300881	1
Caelo	Eucalyptus oil	15063309	1
Caelo	Eucalyptus oil	15400203	2
Caelo	Eucalyptus oil	15400217	1
Caelo	Eucalyptus oil	17337701	1
Caelo	Eucalyptus oil	19016712	1
Caelo	Eucalyptus oil	18171714	1
Caelo	Eucalyptus oil	15400202	3
Caelo	Eucalyptus oil	16351301	1
Caelo	Eucalyptus oil	16351309	1
Caelo	Eucalyptus oil	18171701	1
Caelo	Eucalyptus oil	14039603	1
Caesar & Loretz GmbH Hi…	Eucalyptus oil	15063312	1
Caesar & Loretz GmbH Hi…	Eucalyptus oil	15400203	1
Euro OTC	Eucalyptus oil	1412030-01	1
Bombastus	Eucalyptus oil	305608	1
Kögl	Eucalyptus oil	397311160117	1
Caelo	Eucalyptus oil	16351312	3
Taoasis	Eucalyptus oil	130205-111868	1
Taoasis	Eucalyptus oil	33364-110871	1
Taoasis	Eucalyptus oil	543495-112704	1
Taoasis	Eucalyptus oil	43703-122404	1
Taoasis	Eucalyptus oil	43703-122178	1
Taoasis	Eucalyptus oil	52046-124692	2
Taoasis	Eucalyptus oil	67253-127038	2
Taoasis	Eucalyptus oil	75793-129093	2
Taoasis	Eucalyptus oil	79948-858	1
Taoasis	Eucalyptus oil	82675-1874	1
Taoasis	Eucalyptus oil	91092-3355	2
Taoasis	Eucalyptus oil	98837-4013	1
Taoasis	Eucalyptus oil	98937-4013	1

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Supplier	Substance	Batch	Spectra
Taoasis	Eucalyptus oil	98937-5299	2
Taoasis	Eucalyptus oil	107371-6271	1
Bauer	Niaouli oil	6558611608	1
Caelo	Niaouli oil	16312603	1
Taoasis	Niaouli oil	22553-120413	1
Taoasis	Niaouli oil	22553-120482	1
Taoasis	Niaouli oil	22553-121510	1
Taoasis	Niaouli oil	40428-123092	1
Taoasis	Niaouli oil	40428-128260	4
Taoasis/Noweda	Niaouli oil	5091MGK10	1
Taoasis/Taoasis	Niaouli oil	1500450-5752	1
Bombastus	Rosemary oil	301449	2
Caelo	Rosemary oil	15442017	2
Caelo	Rosemary oil	16276905	1
Caelo	Rosemary oil	16276903	1
Caelo	Rosemary oil	17326714	1
Caelo	Rosemary oil	306506	1
Euro OTC	Rosemary oil	151101602	1
Taoasis	Rosemary oil	26057-122996	1
Taoasis	Rosemary oil	1526-123355	1
Taoasis	Rosemary oil	26057-119164	1
Taoasis	Rosemary oil	1614-125089	12
Taoasis	Rosemary oil	1526-125088	1
Taoasis	Rosemary oil	1862-127716	1
Taoasis	Rosemary oil	1972-773	2
Taoasis	Rosemary oil	1862-128861	1
Taoasis	Rosemary oil	1972-2523	2
Taoasis	Rosemary oil	2331-2821	2
Taoasis	Rosemary oil	2331-6428	1
Taoasis/Taoasis	Rosemary oil	128391-ESJ05	1
Taoasis	Cajeput (essentiel oil)	1724-127033	1
Taoasis	Niaouli oil	1500450-125771	1

- 8454 spectra from 735 *Apo-Ident* customers from a total of 3441 batches from a further 146 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	23 725
Type B	0	400	0	20 401
Type C	0	144	2	8454

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.2308 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 98.5000 %)
Type C	100.0000 % (> 98.7852 %)	98.6301 % (> 96.5753 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rosemary camphor oil	11.16	–
Citus oil	25.94	–
Hyssop oil	28.89	–
Ravensara oil	29.11	–
Myrtle oil	31.68	–
Marjoram oil	39.70	–
Vetiver bourbon oil	42.14	–
Angelica root oil	46.42	–
Sage oil	46.63	–
Cedar wood oil	57.42	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32933	32933	0.00	30.04
31551	31551	0.00	22.02
34104	34104	0.00	24.15
31548	31548	0.00	50.48
34380	34380	0.00	45.39
32903	32903	0.00	31.00

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31136	31136	0.00	57.07
34401	34401	0.00	61.86
32174	32174	0.00	39.86
30966	30966	0.00	38.07
31691	31691	0.00	16.91
34374	34374	0.00	33.82
32970	32970	0.00	45.75
31694	31694	0.00	36.09
31420	31420	0.00	28.89
32173	32173	0.00	56.75
33657	33657	0.00	59.53

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 2.3-2021-01

Validated substance/substance group	**Camphor oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33826-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Camphor oil

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

A sample is considered independent 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 oil	2	1	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan 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 oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Camphor oil	74521-140	33826	40	not required
Taoasis	Camphor oil	944	33827	40	not required

Validation samples

A total of 53 906 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 *Camphor oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Camphor oil*.
- 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
Taoasis	Camphor oil	78793-2563	34039	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Camphor oil*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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 oil* can clearly be 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 oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	40	0	20 761
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Angelica root oil	22.95	–
Marjoram oil	25.25	–
Hyssop oil	32.65	–
Citus oil	38.31	–
Cumin oil	40.82	–
Swiss pine oil	41.49	–
Silver fir oil	42.56	–
Cypress oil	43.56	–
Spruce needle oil	48.48	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33826	33826	0.00	31.35
33827	33827	0.00	30.88

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 2.3-2021-01

Validated substance/substance group	**Cardamom oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33813-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cardamom oil; Cardamom (essential oil)

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cardamom oil	2	1	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cardamom oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Cardamom oil	00897G25	33813	40	not required
Primavera	Cardamom oil	00080M25	33961	40	not required

Validation samples

A total of 53 906 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 *Cardamom oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cardamom oil*.
- 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
Primavera	Cardamom oil	00498H26	34291	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Cardamom oil*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cardamom oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cardamom oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	40	0	20 761
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Cardamom oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citus oil	30.02	–
Vetiver bourbon oil	41.02	–
Manuka oil	43.73	–
Matricaria oil, roman	45.14	–
Sage oil	46.38	–
Cumin oil	52.67	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33961	33961	0.00	46.38
33813	33813	0.00	46.43

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 2.3-2021-01

Validated substance/substance group	**Carrot seed oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31555-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Carrot seed oil; Oleum daucus carota

Special notes

When selecting the *Carrot seed oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Carrot seed oil	3	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Carrot seed oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Carrot seed oil	937-117443	31555	60	not required
Taoasis	Carrot seed oil	1775-125361BAG90451	32812	40	not required
Taoasis	Carrot seed oil	3496IN-K08	34282	40	not required

Validation samples

A total of 53 906 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 *Carrot seed oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Carrot seed oil*.
- 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
Taoasis	Carrot seed oil	26058-119083BAG90451	31636	60
Taoasis	Carrot seed oil	2037	33995	40
Taoasis	Carrot seed oil	1775-125361BAG90451	33203	40

- 20 661 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Carrot seed oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Carrot seed oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Carrot seed oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	140	0	20 661
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 95.7143 %)
Type C	100.0000 % (> 98.8097 %)	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 *Carrot seed oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Marjoram oil	22.08	–
Tea tree oil	27.38	–
Patchouli oil	40.08	–
Thyme oil, white	47.26	–
Lemon grass oil	53.93	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31555	31555	0.00	35.05
34282	34282	0.00	59.28
32812	32812	0.00	64.55

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 2.3-2021-01

Validated substance/substance group	**Cedar wood oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30654-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cedar wood oil; Oleum cedrus deodara

Special notes

When selecting the *Cedar wood oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cedar wood oil	3	3	21

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cedar wood oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Apotheker Bau…	Cedar wood oil	2.880926.1507	31851	60	not required
Taoasis	Cedar wood oil	7891018-121034	31777	60	not required
Taoasis	Cedar wood oil	1627-125061	33199	40	not required

Validation samples

A total of 53 906 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 *Cedar wood oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cedar wood oil*.
- 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
Taoasis	Cedar wood oil	26473-83914BAG90451	30750	40
Taoasis	Cedar wood oil	1627-124623	32268	40
Taoasis	Cedar wood oil	1802-1975	34102	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 22 batches from the substance/substance group *Cedar wood oil*.

- 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
Biofrid / Noweda	Cedar wood oil	17066	1
Taoasis	Cedar wood oil	381008-116967	1
Taoasis	Cedar wood oil	32812-113008	3
Taoasis	Cedar wood oil	7891019-121034	1
Taoasis	Cedar wood oil	7711023-120348	1
Taoasis	Cedar wood oil	831018-122540	1
Taoasis	Cedar wood oil	7891018-120108	1
Taoasis	Cedar wood oil	831018-123089	2
Taoasis	Cedar wood oil	831018-124172	1
Taoasis	Cedar wood oil	1627-125917	1
Taoasis	Cedar wood oil	18302-128288	1
Taoasis	Cedar wood oil	1802-750	3
Taoasis	Cedar wood oil	1627-127827	1
Taoasis	Cedar wood oil	1802-128288	3
Taoasis	Cedar wood oil	1802-1975	1
Taoasis	Cedar wood oil	1802-972	1
Taoasis	Cedar wood oil	2339-3450	1
Taoasis	Cedar wood oil	2339-3615	2
Taoasis	Cedar wood oil	SAP709-5143	1
Taoasis	Cedar wood oil	461016-6429	1
Taoasis/Phönix	Cedar wood oil	3292687	1
Taoasis	Cedar wood oil	1627-125061	2

- 8569 spectra from 736 *Apo-Ident* customers from a total of 3525 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cedar wood oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cedar wood oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	80	40	20 681
Type C	0	31	0	8569

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9455 %)	66.6667 % (> 64.1667 %)
Type C	100.0000 % (> 98.7869 %)	100.0000 % (> 80.6452 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Citus oil	15.66	–
Hyssop oil	20.17	–
Vetiver bourbon oil	22.27	–
Ginger oil	24.25	–
Marjoram oil	25.13	–
Myrtle oil	34.57	–
Yarrow oil	37.14	–
Salmon oil	41.68	–
Angelica root oil	43.39	–
Immortelle oil	43.40	–
Cypress oil	45.89	–
Niaouli oil	49.47	–
Carrot seed oil	49.80	–
Rosemary camphor oil	50.18	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31777	31777	0.00	67.67
33199	33199	0.00	64.69
31851	31851	0.00	20.17

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 2.3-2021-01

Validated substance/substance group	**Chamomile (essential oil)**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33811-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Chamomile (essential oil)

Special notes

When selecting the *Chamomile (essential oil)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Chamomile (essential oil)	4	2	0

Second-stage model

For differentiation of the substance/substance group *Chamomile (essential oil)* the following second-stage model is used:

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Chamomile (essen…	00888G25	33811	40	not required
Primavera	Chamomile (essen…	00715L25	33963	40	not required
Taoasis	Chamomile (essen…	934	33825	30	not required
Taoasis	Chamomile (essen…	2132-1981	33952	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 150 spectra of 4 reference samples from the substance/substance group *Chamomile (essential oil)*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.

- 24 355 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 3 reference samples from the substance/substance group *Chamomile (essential oil)*.

- 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
Primavera	Chamomile (essential oil)	00139C26	34167	40
Taoasis	Chamomile (essential oil)	100477-850	33824	40
Taoasis	Chamomile (essential oil)	934	33825†	10

- 20 711 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Chamomile (essential oil)*.

- 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
Taoasis/Taoasis	Chamomile (essential oil)	2132-1981	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	150	0	24 355
Type B	0	67	23	20 711
Type C	0	1	0	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.0000 %)
Type B	100.0000 % (> 99.9455 %)	74.4444 % (> 71.1111 %)
Type C	100.0000 % (> 98.8499 %)	n/a (n/a)

†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*.

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Bergamot oil	19.63	–
Spearmint oil	33.57	–
Carrot seed oil	43.41	–
Lemon grass oil	49.88	–
Patchouli oil	51.72	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33811	33811	0.00	50.46
33963	33963	0.00	51.24
33825	33825	0.00	22.46
33952	33952	0.00	24.59

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 2.3-2021-01

Validated substance/substance group	**Cinnamon bark oil, Ceylon**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30957-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cinnamon bark oil, Ceylon; Oleum cinnamomi ceylanici

Special notes

When selecting the *Cinnamon bark oil, Ceylon* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cinnamon bark oil, Ceylon	4	1	1

Second-stage model

For differentiation of the substance/substance group *Cinnamon bark oil, Ceylon* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cinnamon bark oil, Ceylon*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Cinnamon bark oi…	00221A27	34375	40	not required
Taoasis	Cinnamon bark oi…	121108-109782BAG90451	30957	40	not required
Taoasis	Cinnamon bark oi…	1311130547-119819	31648	60	not required
Taoasis	Cinnamon bark oi…	415-770	34107	40	not required

Validation samples

A total of 53 906 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 *Cinnamon bark oil, Ceylon*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.

- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cinnamon bark oil, Ceylon*.

- 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
Taoasis	Cinnamon bark oil, Ceylon	415-126411	32791	40
Taoasis	Cinnamon bark oil, Ceylon	415-126411	33202	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 1 batches from the substance/substance group *Cinnamon bark oil, Ceylon*.

- 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
Taoasis	Cinnamon bark oil, Ceylon	415-129078	4

- 8596 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cinnamon bark oil, Ceylon* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cinnamon bark oil, Ceylon* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	4	0	8596

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8011 %)	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 *Cinnamon bark oil, Ceylon* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Siam benzoin	105.08	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
34375	34375	0.00	105.08
30957	30957	0.00	221.19
34107	34107	0.00	177.07
31648	31648	0.00	175.03

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 2.3-2021-01

Validated substance/substance group	**Citric oil / Lime oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31544-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Citric oil / Lime oil; Citric oil; Lime oil; Oleum citri; Oleum citrus aurantifolia

Special notes

When selecting the *Citric oil / Lime oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

A sample is considered independent 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 oil	3	2	47
Lime oil	4	1	3

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan 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 oil / Lime oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Citric oil	D04LI14M-117513	31558	60	not required
Taoasis	Citric oil	3681027-122724	31838	60	not required
Taoasis	Citric oil	127939-ITJ04	33611	40	not required
Primavera	Lime oil	00182A27	34393	80	not required
Taoasis	Lime oil	059-117571	31544	60	not required
Taoasis	Lime oil	15506-1458	33874	40	not required
Taoasis	Lime oil	15506-1762	33942	40	not required

Validation samples

A total of 53 906 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 *Citric oil / Lime oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 7 different batches.
- 24 125 spectra from a total of 497 batches from further 159 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 260 spectra of 6 reference samples from the substance/substance group *Citric oil / Lime oil*.
- 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
Primavera	Citric oil	00011A27	34379	40
Taoasis	Citric oil	03LI16M-125453I09	32771	40
Taoasis	Lime oil	867-124956	32800	40
Taoasis	Citric oil	03LI16M-125453I09	32941	40
Taoasis	Lime oil	059-117571	31654	60
Taoasis	Lime oil	867-124956	32976	40

- 20 541 spectra from a total of 443 batches from further 202 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 59 *Apo-Ident* customers from 51 batches from the substance/substance group *Citric oil / Lime oil*.

- Among them are spectra of independent samples from 50 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
bergland	Citric oil	K703167	1
Bergland	Citric oil	K603901	1
Bombastus	Citric oil	302311	1
Bombastus	Citric oil	301912	1
Bombastus	Citric oil	18006427	1
Bombastus	Citric oil	19002045	1
Bombastus	Citric oil	304030	1
Bombastus	Citric oil	15F29-B04-325354	1
Bombastus	Citric oil	19003228	1
Bombastus	Citric oil	297506	1
Bombastus	Citric oil	12268005-1-0	1
Bombastus	Citric oil	19003199	1
Caelo	Citric oil	14365212	3
Caelo	Citric oil	16028702	3
Caelo	Citric oil	15182711	1
Caelo	Citric oil	16275206	1
Caelo	Citric oil	16028719	2
Caelo	Citric oil	16275202	1
Caelo	Citric oil	2416Q-01973	1
Caelo	Citric oil	16275213	1
Caelo	Citric oil	17321104	2
Caelo	Citric oil	18092216	1
Caelo	Citric oil	16275216	3
Caelo	Citric oil	18092202	3
Caelo	Citric oil	91(18092216)	1
Caelo	Citric oil	15182703	3
Caelo	Citric oil	14385201	1
Caelo	Citric oil	W373	1
Caelo	Citric oil	18328003	4
Fagron	Citric oil	14H06-B02-308273	1
Fagron	Citric oil	13K14-B03-294704	1
Fagron	Citric oil	14H06-B02-299949	1

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Supplier	Substance	Batch	Spectra
Fagron	Citric oil	15f29-b04-325354	1
Fagron	Citric oil	15F29-804	1
Fagron	Citric oil	17B14-B04	1
Fagron	Citric oil	15F29-B04-325354	1
Fagron	Citric oil	15F29-B04-330854	1
Fagron	Citric oil	17B14-B04-334835	1
Fagron	Citric oil	17B14-B04-350559	1
Fagron	Citric oil	17B14-B04-352490	1
Fagron	Citric oil	19K11-F08	1
Fagron	Citric oil	15F29-B04	2
Caelo	Citric oil	17106807	3
Fagron	Citric oil	15F29-B04-322985	1
Kögl	Citric oil	182006163916	1
Fagron	Citric oil	17B14B04341736	1
Sanacorp	Citric oil	15182703	1
Taoasis	Citric oil	3681003-124333	1
Taoasis	Citric oil	E160576-127218	1
Taoasis	Citric oil	W160567-127218	1
Taoasis	Lime oil	867-124956	2
Taoasis	Lime oil	867-127657	1
Taoasis/Sanaorp	Lime oil	867_124704I05	1
Taoasis/Taoasis	Lime oil	867-124956	1

- 8527 spectra from 731 *Apo-Ident* customers from a total of 3495 batches from a further 148 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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 oil / Lime oil* can clearly be 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 oil / Lime oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 125
Type B	0	239	21	20 541
Type C	0	72	1	8527

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9600 %)	100.0000 % (> 98.4211 %)
Type B	100.0000 % (> 99.9453 %)	91.9231 % (> 90.7692 %)
Type C	100.0000 % (> 98.7857 %)	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 *Citric oil / Lime oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Mandarin oil, green	17.69	–
Grapefruit oil, organic	20.04	–
Orange oil	33.06	–
Silver fir oil	38.76	–
Tea tree oil	47.99	–
Blood orange oil	56.48	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33942	33942	0.00	40.79
34393	34393	0.00	30.63
33874	33874	0.00	41.50
31544	31544	0.00	38.76
31558	31558	0.00	17.71
31838	31838	0.00	17.41
33611	33611	0.00	17.11

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 2.3-2021-01

Validated substance/substance group	**Citronella oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31550-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Citronella oil; Oleum cymbopogon winterianus

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Citronella oil	4	2	4

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Citronella oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Citronella oil	00671A27	34409	40	not required
Taoasis	Citronella oil	140121-115623	31550	60	not required
Taoasis	Citronella oil	1291021-122850	31840	60	not required
Taoasis	Citronella oil	1794-373	33728	40	not required

Validation samples

A total of 53 906 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 *Citronella oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Citronella oil*.
- 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
Taoasis	Citronella oil	108494-126305	32798	40
Taoasis	Citronella oil	108494-126776	33047	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Citronella oil*.
- 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
Apotheker Bauer und Cie…	Citronella oil	7444171705	1
Bombastus	Citronella oil	19001887	1
Kögl	Citronella oil	228107163016	1
Taoasis	Citronella oil	5211028-120284	1

- 8596 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Citronella oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Citronella oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	80	0	20 721
Type C	0	4	0	8596

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8011 %)	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 *Citronella oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rose-geranium oil, organic	30.44	–
alpha-bisabolol (racemic) at least 85%	41.38	–
Palmarosa oil, organic	43.15	–
Lemon grass oil	43.94	–
Marjoram oil	47.10	–
Tea tree oil	48.46	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31550	31550	0.00	35.09
31840	31840	0.00	38.94
33728	33728	0.00	34.72
34409	34409	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 2.3-2021-01

Validated substance/substance group	**Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrai**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30961-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil; Citus oil; Clary sage oil; Hyssop oil; Lavender oil; Myrtle oil; Oleum citrus aurantium; Oleum hyssopus officinalis; Oleum lavendula officinalis; Oleum salviae sclarea; Petitgrain oil

Special notes

When selecting the *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Citus oil	4	2	2
Clary sage oil	3	3	6
Hyssop oil	4	2	1
Lavender oil	4	4	54
Myrtle oil	3	2	0
Petitgrain oil	3	2	0

Second-stage model

For differentiation of the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Citus oil	00438D25	33760	40	not required
Primavera	Citus oil	00621G26	34294	40	not required
Primavera	Citus oil	00673L26	34395	40	not required
Taoasis	Citus oil	788	33816	40	not required
Primavera	Clary sage oil	00529M26	34367	40	not required
Taoasis	Clary sage oil	2098-115222	31669	60	not required
Taoasis	Clary sage oil	1834-127059	33033	40	not required
Apotheker Bau…	Hyssop oil	13.201345120.16.02	31850	60	not required
Taoasis	Hyssop oil	31823-118643	31649	60	not required
Taoasis	Hyssop oil	33065-122200	31782	60	not required
Taoasis	Hyssop oil	1616260-125049	32980	40	not required
Primavera	Lavender oil	00684K25	33804	40	not required
Taoasis	Lavender oil	L16812DN-108661BAG90451	30961	40	not required
Taoasis	Lavender oil	110186BAG90451	30962	40	not required
Taoasis	Lavender oil	22015-121843	31756	60	not required
Primavera	Myrtle oil	00401D25	33797	40	not required
Primavera	Myrtle oil	00877L25	33957	40	not required
Taoasis	Myrtle oil	013	33830	40	not required
Apotheker Bau…	Petitgrain oil	6.56267.16.02	31852	60	not required
Taoasis	Petitgrain oil	26056-120864	31778	60	not required
Taoasis	Petitgrain oil	4031015-126048	33024	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 980 spectra of 21 reference samples from the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 21 different batches.

- 23 525 spectra from a total of 483 batches from further 155 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 720 spectra of 18 reference samples from the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil*.
- Among them are spectra of independent samples from 15 batches from which no spectra 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
Primavera	Citus oil	00348C26	34178	40
Taoasis	Citus oil	1510-135	33817	40
Taoasis	Clary sage oil	487962-107805BAG90451	30749	40
Taoasis	Clary sage oil	10140-145	33871	40
Taoasis	Clary sage oil	1834-129098	34284	40
Apotheker Bauer & Cie	Hyssop oil	13.201604082.17.01	32923	40
Taoasis	Hyssop oil	1616260-1982	34110	40
Primavera	Lavender oil	00793A26	33953	40
Primavera	Lavender oil	00184G26	34165	40
Taoasis	Lavender oil	2/2015-125808I09	33015	40
Taoasis	Lavender oil	22015-125925I10	33016	40
Primavera	Myrtle oil	00971J25	33807	40
Primavera	Myrtle oil	00392M26	34384	40
Taoasis	Petitgrain oil	29551-105402BAG90451	30752	40
Taoasis	Petitgrain oil	4031015-147	34108	40
Taoasis	Clary sage oil	2098-115222	32797	40
Taoasis	Clary sage oil	10140-145	33943	40
Taoasis	Petitgrain oil	4031015-126048	33025	40

- 20 081 spectra from a total of 430 batches from further 198 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 103 spectra from 45 *Apo-Ident* customers from 64 batches from the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil*.
- 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
Taoasis	Citus oil	1510-1171	1
Taoasis	Citus oil	2345-2578	2

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Supplier	Substance	Batch	Spectra
Taoasis	Clary sage oil	487962-106655	1
Taoasis	Clary sage oil	2098-119159	1
Taoasis	Clary sage oil	1700-125289	2
Taoasis	Clary sage oil	13304-5798	2
Taoasis	Clary sage oil	10140-146	1
Taoasis	Clary sage oil	13304-6656	1
Taoasis	Hyssop oil	31095-105392	1
Bergland	Lavender oil	K502790	1
Bombastus	Lavender oil	300666	1
Bombastus	Lavender oil	18000582	1
Bombastus	Lavender oil	19004173	1
Bombastus	Lavender oil	19001102	2
Bombastus	Lavender oil	80311204	1
Caelo	Lavender oil	16292205	1
Caelo	Lavender oil	16292211	2
Caelo	Lavender oil	18128204	2
Caelo	Lavender oil	18219005	1
Caelo	Lavender oil	16023001	1
Caelo	Lavender oil	15278105	1
Caelo	Lavender oil	17132711	5
Caelo	Lavender oil	16292214	1
Caelo	Lavender oil	16023017	1
Caelo	Lavender oil	16292216	2
Caelo	Lavender oil	18128202	1
Caelo	Lavender oil	18128203	1
Caelo	Lavender oil	1010548	2
Cordes/Noweda	Lavender oil	16023002	1
Fagron	Lavender oil	16H01-B04	1
Euro OTC	Lavender oil	1710038-02	1
Euro OTC	Lavender oil	1706003-01	1
Fagron	Lavender oil	18K19-B01	1
Fagron	Lavender oil	19B20-B01-191698	1
Fagron	Lavender oil	17G20-B07-342691	2
Bombastus	Lavender oil	305279	1
Bombastus	Lavender oil	303303	1
Caelo	Lavender oil	18219011	1
Primavera	Lavender oil	1078C23	1
Primavera	Lavender oil	471A27	1
Primavera/Noweda	Lavender oil	378E25	1
Primavera/Phoenix	Lavender oil	326C26	1
Taoasis	Lavender oil	4651010	1
Taoasis	Lavender oil	22015-125927	2
Taoasis	Lavender oil	34/151/16	1
Taoasis	Lavender oil	2/2015-125808I09	12
Taoasis	Lavender oil	22015-126998	3
Taoasis	Lavender oil	22015-508	5
Taoasis	Lavender oil	22015-128587	1
Taoasis	Lavender oil	2015-2394	3
Taoasis	Lavender oil	16082301/2016-2908	1
Taoasis	Lavender oil	16082301/2016/2908	1
Taoasis	Lavender oil	16082301/2016-2909	4
Taoasis	Lavender oil	106082301/2016-2909	1
Taoasis	Lavender oil	160802301/2016-1909	1
Taoasis	Lavender oil	170124022016-5298	1
Taoasis	Lavender oil	96336-5473	2
Taoasis	Lavender oil	170001022016-5298	1
Taoasis	Lavender oil	S05-18-6464	3
Taoasis	Lavender oil	109744-6805	1
Taoasis	Lavender oil	6981BG-L05	1
Taoasis/Noweda	Lavender oil	16716-126380/11	1

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Supplier	Substance	Batch	Spectra
Taoasis/Taoasis	Lavender oil	L665-5037	1
Taoasis	Clary sage oil	2098-115222	1

- 8497 spectra from 730 *Apo-Ident* customers from a total of 3482 batches from a further 146 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	980	0	23 525
Type B	0	710	10	20 078
Type C	0	103	0	8497

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.3878 %)
Type B	100.0000 % (> 99.9456 %)	98.6111 % (> 98.1944 %)
Type C	100.0000 % (> 98.7854 %)	100.0000 % (> 94.1748 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Ravensara oil	20.22	–
Neroli oil	29.03	–

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Substanz	Distance in main model	Distance in second-stage model
Melissa oil 30%	29.99	–
Marjoram oil	31.35	–
Cypress oil	31.80	–
Cedar wood oil	32.09	–
Angelica root oil	32.52	–
Rosemary camphor oil	35.23	–
Thyme oil, white	37.86	–
Vetiver bourbon oil	38.74	–
Sage oil	39.15	–
Yarrow oil	40.79	–
Ginger oil	43.73	–
Niaouli oil	45.69	–
Coriander oil	46.98	–
Rosemary oil	50.74	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Citus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31669	31669	0.00	52.46
33033	33033	0.00	53.93
31782	31782	0.00	42.75
31649	31649	0.00	41.36
31852	31852	0.00	33.59
33804	33804	0.00	71.82
31778	31778	0.00	74.14
33024	33024	0.00	64.02
32980	32980	0.00	20.22
33830	33830	0.00	44.18
34367	34367	0.00	80.52
34395	34395	0.00	34.25
31850	31850	0.00	42.08
30962	30962	0.00	66.03
31756	31756	0.00	72.74
33760	33760	0.00	39.90
33816	33816	0.00	32.09
34294	34294	0.00	33.34
30961	30961	0.00	52.24
33797	33797	0.00	34.60
33957	33957	0.00	35.99

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 2.3-2021-01

Validated substance/substance group	**Clove oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31270-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Clove oil; Oleum caryophylli

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Clove oil	4	1	10

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Clove oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bombastus	Clove oil	279132	31035	40	not required
Caelo	Clove oil	12380605	31270	40	not required
Taoasis	Clove oil	2891012-116936	31557	60	not required
Taoasis	Clove oil	1426-120481	31683	60	not required

Validation samples

A total of 53 906 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 *Clove oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Clove oil*.
- 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
Taoasis	Clove oil	1598-124689	32938	40
Taoasis	Clove oil	1598-124689	32940	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 batches from the substance/substance group *Clove oil*.
- 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	Clove oil	15402108	1
Caelo	Clove oil	15316102	1
Caelo	Clove oil	19066804	1
Caelo	Clove oil	17354205	2
Caelo	Clove oil	15316103	1
Caelo	Clove oil	15402109	1
Caelo	Clove oil	18178005	1
Caelo	Clove oil	15119304	1
Primavera	Clove oil	47G24	1
Primavera/Sanacorp	Clove oil	133A25	1

- 8589 spectra from 735 *Apo-Ident* customers from a total of 3536 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Clove oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Clove oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	80	0	20 721
Type C	0	10	1	8589

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7907 %)	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 *Clove oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Siam benzoin	423.92	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31557	31557	0.00	423.92
31683	31683	0.00	430.80
31035	31035	0.00	441.25
31270	31270	0.00	441.22

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 2.3-2021-01

Validated substance/substance group	**Common wormwood oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30842-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Common wormwood oil; Oleum artemisia vulgaris

Special notes

When selecting the *Common wormwood oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Common wormwood oil	2	2	1

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Common wormwood oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
ASAV Apotheke...	Common wormwood ...	10116310555	31637	60	not required
ASAV Apotheke...	Common wormwood ...	10409310558	34209	40	not required

Validation samples

A total of 53 906 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 *Common wormwood oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 405 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Common wormwood oil*.
- 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
ASAV Apotheken-Service	Common wormwood oil	10815310556	32770	40
Taoasis	Common wormwood oil	7.9363	30842	40

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Supplier	Substance	Batch	Sample ID	Spectra
ASAV Apotheken-Service	Common wormwood oil	10815310556	33013	40
ASAV Apotheken-Service	Common wormwood oil	10815310556	33600	40
ASAV Apotheken-Service	Common wormwood oil	10815310556	33851	40

- 20 601 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Common wormwood oil*.

- 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	Common wormwood oil	79363	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Common wormwood oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Common wormwood oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 405
Type B	0	52	148	20 601
Type C	0	0	1	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9454 %)	26.0000 % (> 24.5000 %)
Type C	100.0000 % (> 98.8499 %)	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 *Common wormwood oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Thuja oil	55.14	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31637	31637	0.00	68.49
34209	34209	0.00	82.82

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 2.3-2021-01

Validated substance/substance group	**Contramarum aroma**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31007-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Contramarum aroma; Contramarum flavour

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Contramarum aroma	3	3	60

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Contramarum aroma*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Contramarum aroma	13141605	31007	40	1403096
Caelo	Contramarum aroma	13411002	31289	40	not required
Caelo	Contramarum aroma	13411007	31398	40	not required

Validation samples

A total of 53 906 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 *Contramarum aroma*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 385 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Contramarum aroma*.
- 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	Contramarum aroma	162671	32695	40
Caelo	Contramarum aroma	172230	33701	40
Caelo	Contramarum aroma	181067	34066	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 152 spectra from 67 *Apo-Ident* customers from 61 batches from the substance/substance group *Contramarum aroma*.

- 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
Alliance Healthcare	Contramarum aroma	17223007	1
Cael	Contramarum aroma	13141603	1
Caelo	Contramarum aroma	11378804	1
Caelo	Contramarum aroma	12201407	2
Caelo	Contramarum aroma	7071207	1
Caelo	Contramarum aroma	7091302	1
Caelo	Contramarum aroma	134111002	1
Caelo	Contramarum aroma	2041515	1
Caelo	Contramarum aroma	21051508	1
Caelo	Contramarum aroma	14320005	1
Caelo	Contramarum aroma	15113011	1
Caelo	Contramarum aroma	16083806	1
Caelo	Contramarum aroma	16267102	4
Caelo	Contramarum aroma	16083805	1
Caelo	Contramarum aroma	17223002	4
Caelo	Contramarum aroma	19121701	1
Caelo	Contramarum aroma	17223005	3
Caelo	Contramarum aroma	17223007	5
Caelo	Contramarum aroma	12051808	1
Caelo	Contramarum aroma	30081804	1
Caelo	Contramarum aroma	19209401	4
Caelo	Contramarum aroma	13815152	1
Caelo	Contramarum aroma	13141608	2
Caelo	Contramarum aroma	22(18106701)	1
Caelo	Contramarum aroma	23(19065401)	1
Caelo	Contramarum aroma	13411011	1
Caelo	Contramarum aroma	19209402	1
Caelo	Contramarum aroma	7082006	1
Caelo	Contramarum aroma	14320015	3
Caelo	Contramarum aroma	16083804	2
Caelo	Contramarum aroma	13141606	3
Caelo	Contramarum aroma	14320006	3
Caelo	Contramarum aroma	1315Q-03148	1
Caelo	Contramarum aroma	5315A-03148	1
Caelo	Contramarum aroma	4916E-03148	1
Caelo	Contramarum aroma	19065401	11
Caelo	Contramarum aroma	19209403	2
Caelo	Contramarum aroma	21(17223001)	1
Caelo	Contramarum aroma	16267101	5
Caelo	Contramarum aroma	14320001	1
Caelo	Contramarum aroma	16267103	4

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Supplier	Substance	Batch	Spectra
Caelo	Contramarum aroma	17223001	7
Caelo	Contramarum aroma	14320009	2
Caelo	Contramarum aroma	143200009	1
Caelo	Contramarum aroma	15113003	2
Caelo	Contramarum aroma	16083802	2
Caelo	Contramarum aroma	19129002	1
Caelo	Contramarum aroma	169267103	1
Caelo	Contramarum aroma	18106702	6
Caelo	Contramarum aroma	18106703	7
Caelo	Contramarum aroma	19065403	3
Caelo	Contramarum aroma	18106706	1
Caelo	Contramarum aroma	15113002	2
Caelo	Contramarum aroma	18106705	1
Caelo	Contramarum aroma	19129001	3
Caelo	Contramarum aroma	192009401	1
Caesar & Loretz GmbH	Contramarum aroma	19065403	4
Caesar & Loretz GmbH	Contramarum aroma	19129001	1
Caesar & Loretz GmbH	Contramarum aroma	19129002	1
Caesar & Loretz GmbH	Contramarum aroma	19209403	1
Fagron	Contramarum aroma	16083801	1
Fiebig	Contramarum aroma	11378810	1
Gehe	Contramarum aroma	12201404	1
Caelo	Contramarum aroma	16083801	8
Caelo	Contramarum aroma	17223004	4
Phoenix Goettin	Contramarum aroma	70401432001	1
VDL; 18.07.15; 6,56EUR	Contramarum aroma	14320005	1
VDL;02.01.15;6,42EUR	Contramarum aroma	14320001	1
Caelo	Contramarum aroma	13411007	4

- 8448 spectra from 729 *Apo-Ident* customers from a total of 3485 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Contramarum aroma* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Contramarum aroma* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	117	3	20 681
Type C	0	134	18	8448

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9455 %)	97.5000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7852 %)	88.1579 % (> 86.1842 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Raspberry aroma	41.65	–
Strawberry aroma	110.10	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31007	31007	0.00	59.42
31289	31289	0.00	55.51
31398	31398	0.00	58.19

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 2.3-2021-01

Validated substance/substance group	**Cumin oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30449-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cumin oil; Oleum cuminum cyminum

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cumin oil	2	2	4

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cumin oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Cumin oil	130910-113031BAG90451	31141	40	not required
Taoasis	Cumin oil	51764-124375	32267	40	not required
Taoasis	Cumin oil	51764-124375	32904	40	not required

Validation samples

A total of 53 906 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 *Cumin oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 385 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cumin oil*.
- 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
Taoasis	Cumin oil	2016109952-127656	33841	40
Taoasis	Cumin oil	2016109952-128855	33873	40
Taoasis	Cumin oil	51764-124375	32266	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Cumin oil*.

- 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
Taoasis	Cumin oil	24081-106027	1
Taoasis	Cumin oil	121217-111221	1
Taoasis	Cumin oil	104723-298	1
Taoasis/Noweda	Cumin oil	51764-124373BAG9045	1

- 8596 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cumin oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cumin oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	120	0	20 681
Type C	0	3	1	8596

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8011 %)	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 *Cumin oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Marjoram oil	132.53	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31141	31141	0.00	142.55
32267	32267	0.00	140.07
32904	32904	0.00	145.28

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 2.3-2021-01

Validated substance/substance group	**Cypress oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30457-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Cypress oil; Oleum cupressus sempervirens

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Cypress oil	4	3	14

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Cypress oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Cypress oil	00177G25	33802	40	not required
Primavera	Cypress oil	00403L25	33954	40	not required
Taoasis	Cypress oil	732-119820	31656	60	not required
Taoasis	Cypress oil	43953-129229	33623	40	not required

Validation samples

A total of 53 906 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 *Cypress oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Cypress oil*.
- 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
Primavera	Cypress oil	00586C26	34169	40
Primavera	Cypress oil	00660L26	34394	40
Taoasis	Cypress oil	107527-125443	32806	40

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Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Cypress oil	107527-125443	33045	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 15 batches from the substance/substance group *Cypress oil*.
- 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
Taoasis	Cypress oil	487749-108547	1
Taoasis	Cypress oil	514085-111139	1
Taoasis	Cypress oil	487749-107790	1
Taoasis	Cypress oil	33720-115882	1
Taoasis	Cypress oil	33720-118623	1
Taoasis	Cypress oil	33720-118895	2
Taoasis	Cypress oil	1039-121894	3
Taoasis	Cypress oil	1039-122434	1
Taoasis	Cypress oil	107527-125965	1
Taoasis	Cypress oil	341012-123298	1
Taoasis	Cypress oil	107527-125443	2
Taoasis	Cypress oil	107527-27014	1
Taoasis	Cypress oil	107527-127323	6
Taoasis	Cypress oil	45953-129229	1
Taoasis	Cypress oil	43953-129229	1

- 8576 spectra from 736 *Apo-Ident* customers from a total of 3531 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Cypress oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Cypress oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	148	12	20 641
Type C	0	23	1	8576

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9454 %)	92.5000 % (> 90.6250 %)
Type C	100.0000 % (> 98.7875 %)	95.8333 % (> 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 *Cypress oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Marjoram oil	30.24	–
Citus oil	30.32	–
Myrtle oil	34.32	–
Ginger oil	48.48	–
Carrot seed oil	51.00	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33802	33802	0.00	49.37
33954	33954	0.00	49.85
31656	31656	0.00	71.16
33623	33623	0.00	68.89

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 2.3-2021-01

Validated substance/substance group	**Dermatop® base ointment**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31060-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dermatop® base ointment

Special notes

When selecting the *Dermatop® base ointment* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dermatop® base ointment	2	2	31

Second-stage model

For differentiation of the substance/substance group *Dermatop® base ointment* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Dermatop® base ointment*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Sanofi aventis	Dermatop® base o…	3F052A	31060	40	not required
Sanofi aventis	Dermatop® base o…	5F080A	31717	60	not required

Validation samples

A total of 53 906 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 *Dermatop® base ointment*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 405 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Dermatop® base ointment*.
- 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
Sanofi aventis	Dermatop® base ointment	5F089A	32718	40
Sanofi aventis	Dermatop® base ointment	7F106A	33965	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 17 *Apo-Ident* customers from 32 batches from the substance/substance group *Dermatop® base ointment*.

- 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	Dermatop® base ointment	5F080A	1
Caelo	Dermatop® base ointment	8F124A	1
Caelo	Dermatop® base ointment	7F107A	1
Phönix	Dermatop® base ointment	7F108B	1
Sanacorp/ Sanofi	Dermatop® base ointment	9F128A	1
Sanacorp/Sanofi WE:22.0...	Dermatop® base ointment	5F086A	1
Sanofi	Dermatop® base ointment	8F116A	1
Sanofi	Dermatop® base ointment	9F178A	1
Sanofi	Dermatop® base ointment	9F129A	2
Sanofi - Noweda	Dermatop® base ointment	5F089A	1
Sanofi / Alliance Healt...	Dermatop® base ointment	6F094A	1
Sanofi / Gehe	Dermatop® base ointment	6F099A	1
Sanofi / Sanacorp	Dermatop® base ointment	8F125A	1
Sanofi /Noweda	Dermatop® base ointment	8F121A	1
Sanofi /Noweda	Dermatop® base ointment	0F135A	1
Sanofi /Noweda	Dermatop® base ointment	0F137A	1
Sanofi/Alliance	Dermatop® base ointment	8F119A	1
Sanofi/Gehe	Dermatop® base ointment	5F078A	1
Sanofi/GEHE	Dermatop® base ointment	8F117A	1
Sanofi/GEHE	Dermatop® base ointment	8F116A	1
Sanofi/GEHE	Dermatop® base ointment	8F115A	1
Sanofi/GEHE	Dermatop® base ointment	8F126A	1
Sanofi/Kehr	Dermatop® base ointment	6F094A	1
Sanofi/Kehr	Dermatop® base ointment	6F099A	1
Sanofi/Phönix	Dermatop® base ointment	7F105A	1
Sanofi/Phönix	Dermatop® base ointment	7F109A	2
Sanofi/Phönix	Dermatop® base ointment	8F114A	1
Sanofi/Phönix	Dermatop® base ointment	8F113A	1
Sanofi/Phönix	Dermatop® base ointment	8F116A	1
Sanofi/Phönix	Dermatop® base ointment	8F119A	2
Sanofi/Phönix	Dermatop® base ointment	8F118B	1
Sanofi/Phönix	Dermatop® base ointment	8F121A	3
Sanofi/Phönix	Dermatop® base ointment	8F125A	2
Sanofi/Phönix	Dermatop® base ointment	8F1238	1
Sanofi/Phönix	Dermatop® base ointment	8F126A	1
Sanofi/Phönix	Dermatop® base ointment	9F127A	1
Sanofi/Phönix	Dermatop® base ointment	9F131A	1
Sanofi/Phönix	Dermatop® base ointment	9F134A	1
Sanofi/Phönix	Dermatop® base ointment	F137A	1
Sanofi-Aventis	Dermatop® base ointment	7F103A	1

- 8554 spectra from 736 *Apo-Ident* customers from a total of 3514 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Dermatop® base ointment* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dermatop® base ointment* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 405
Type B	0	80	0	20 721
Type C	0	45	1	8554

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7862 %)	97.8261 % (> 91.3043 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dermatop® base ointment* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Linola® H fat N	19.45	–
Excipial® lipo cream	20.42	–
Linola® fat cream	22.92	–
Alfason Basis Cresa®	28.15	–
Alfason® Repair	36.82	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dermatop® base ointment* is separated from critical neighbours in a second-

stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31717	31717	0.00	24.91
31060	31060	0.00	21.33

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 2.3-2021-01

Validated substance/substance group	**Dexeryl®**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31512-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dexeryl®

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dexeryl®	3	2	16

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Dexeryl®*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Pierre Fabre	Dexeryl®	G99016	31512	60	not required
Pierre Fabre	Dexeryl®	G00419	31630	60	not required
Pierre Fabre	Dexeryl®	G00650	33635	40	not required

Validation samples

A total of 53 906 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 *Dexeryl®*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Dexeryl®*.
- 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
Pierre Fabre	Dexeryl®	G00623	32762	40
Pierre Fabre	Dexeryl®	G00658	33945	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 5 *Apo-Ident* customers from 16 batches from the substance/substance group *Dexeryl*®.
- 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
Noweda	Dexeryl®	G00909	1
PiereFabre/Now	Dexeryl®	G00577	1
Pierre Fabre / phoenix	Dexeryl®	600869	1
Pierre Fabre /Noweda	Dexeryl®	Goo606	1
Pierre Fabre/Sanacorp	Dexeryl®	G00729	2
Pierre Fabre/Sanacorp	Dexeryl®	G00064_A	1
PierreFabre/ Phoenix	Dexeryl®	G00835	1
PierreFabre/ Phoenix	Dexeryl®	G00904	1
PierreFabre/ Phoenix	Dexeryl®	G00966	2
PierreFabre/ Phoenix	Dexeryl®	G00967	2
PierreFabre/ Phoenix	Dexeryl®	G00956/2x500g	1
PierreFabre/ Phoenix	Dexeryl®	G01021	2
PierreFabre/ Phoenix	Dexeryl®	G01088	1
PierreFabre/ Phoenix	Dexeryl®	G01118	1
PierreFabre/ Phoenix	Dexeryl®	G01117	1
PierreFabre/ Phoenix	Dexeryl®	G01122	1

- 8580 spectra from 735 *Apo-Ident* customers from a total of 3530 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Dexeryl*® can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dexeryl*® and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	80	0	20 721
Type C	0	20	0	8580

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7880 %)	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 *Dexeryl*® in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neuroderm® moisturising cream	16.52	–
Neuroderm® care lotion	19.79	–
Base cream Taoasis	20.42	–
Excipial® U10 Lipolotio	22.79	–
Hans Karrer Lipolotion MicroSilver	27.88	–
Dimeticone ointment 10% SR	30.03	–
Eucerinum O/W basis	30.35	–
Abitima® clinic body cream	32.38	–
Neribas® cream	33.45	–
Asche Basis® lotion	34.37	–
DMS® base cream high classic	35.18	–
DMS® base cream high classic plus	35.48	–
Abitima® clinic face cream	37.08	–
La Roche-Posay Toleriane	37.36	–
Fabitop® base cream	37.86	–
DMS® base cream classic	39.92	–
Eucerinum W/O basis	43.05	–
Asche Basis® cream	44.20	–
Hans Karrer Lipocream MicroSilver	44.37	–
Optiderm® lotion	44.98	–
Linola® body milk	45.14	–
Allergika® Base cream	50.07	–

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33635	33635	0.00	24.77
31512	31512	0.00	20.51
31630	31630	0.00	27.81

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 2.3-2021-01

Validated substance/substance group	**Dichloroacetic acid**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30417-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dichloroacetic acid; Acidum dichloraceticum

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dichloroacetic acid	3	1	0

Second-stage model

For differentiation of the substance/substance group *Dichloroacetic 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 *Dichloroacetic acid*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Merck	Dichloroacetic a…	S6674841451	31642	60	not required
Merck	Dichloroacetic a…	S6674841614	32750	40	not required
Merck	Dichloroacetic a…	S7209041737	33794	40	not required

Validation samples

A total of 53 906 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 *Dichloroacetic acid*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Dichloroacetic 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
Merck	Dichloroacetic acid	S7209241824	34185	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Dichloroacetic 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Dichloroacetic 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 *Dichloroacetic 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	24 365
Type B	0	10	30	20 761
Type C	0	0	0	8600

The substance/substance group *Dichloroacetic 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 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9460 %)	25.0000 % (> 17.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Dichloroacetic acid* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Nicotine	164.00	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dichloroacetic 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
33794	33794	0.00	229.60
31642	31642	0.00	221.03
32750	32750	0.00	213.34

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 2.3-2021-01

Validated substance/substance group	**Dimeticone ointment 10% SR / Optiderm® lotion**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31243-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dimeticone ointment 10% SR / Optiderm® lotion; Dimeticone ointment 10% SR; Optiderm® lotion; Unguentum dimeticoni 10% SR

Special notes

When selecting the *Dimeticone ointment 10% SR / Optiderm® lotion* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dimeticone ointment 10% SR	3	1	27
Optiderm® lotion	3	1	0

Second-stage model

For differentiation of the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
apomix	Dimeticone ointm…	08B041213	31243	30	not required
apomix	Dimeticone ointm…	10A181214	31638	60	not required
apomix	Dimeticone ointm…	11A271216	33041	40	not required
Almirall	Optiderm® lotion	341431	31266	40	not required
Almirall	Optiderm® lotion	511951	31759	60	not required
Almirall	Optiderm® lotion	706961	33268	40	not required

Validation samples

A total of 53 906 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 *Dimeticone ointment 10% SR / Optiderm® lotion*. These samples are listed above in the *calibration samples* section. The reference samples come from 6 different batches.

- 24 235 spectra from a total of 498 batches from further 159 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 3 reference samples from the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion*.

- 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
apomix	Dimeticone ointment 10% SR	10A021117	33870	40
Almirall	Optiderm® lotion	633771	32757	20
Almirall	Optiderm® lotion	706961	33267	40

- 20 701 spectra from a total of 444 batches from further 202 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 29 batches from the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion*.

- 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
Apomix	Dimeticone ointment 10% SR	3B180214	1
Apomix	Dimeticone ointment 10% SR	3A220316	1
Apomix	Dimeticone ointment 10% SR	2B150317	1
Apomix	Dimeticone ointment 10% SR	11a271216	1
Apomix	Dimeticone ointment 10% SR	9B041017	1
Apomix	Dimeticone ointment 10% SR	11B031117	1
Apomix	Dimeticone ointment 10% SR	5A210618	3
Apomix	Dimeticone ointment 10% SR	9A051218	1
Apomix	Dimeticone ointment 10% SR	1A150119	1
Apomix	Dimeticone ointment 10% SR	4A230519	2
Apomix	Dimeticone ointment 10% SR	5A200619	1
apomix/Gehe	Dimeticone ointment 10% SR	6A190614	1
apomix/Gehe	Dimeticone ointment 10% SR	10A181214	1
apomix/Holdermann	Dimeticone ointment 10% SR	1A150115	1
apomix/Holdermann	Dimeticone ointment 10% SR	8A090915	1
apomix/Holdermann	Dimeticone ointment 10% SR	1A120116	1
apomix/Holdermann	Dimeticone ointment 10% SR	6A300616	1
apomix/Holdermann	Dimeticone ointment 10% SR	4A080414	1
apomix/Phönix	Dimeticone ointment 10% SR	4A010415	1
apomix/Phönix	Dimeticone ointment 10% SR	5A020616	1
apomix/Phönix	Dimeticone ointment 10% SR	7A170816	1
apomix/Phönix	Dimeticone ointment 10% SR	1A070217	1
apomix/Phönix	Dimeticone ointment 10% SR	7A310718	1
apomix/Phönix	Dimeticone ointment 10% SR	1A150119	1
apomix/Phönix	Dimeticone ointment 10% SR	2A260219	1
apomix/Phönix	Dimeticone ointment 10% SR	7A151019	1
apomix/Phönix	Dimeticone ointment 10% SR	2A180220	1
apomix/Phönix	Dimeticone ointment 10% SR	5A130520	1
Apomix/Phönix	Dimeticone ointment 10% SR	8A041213	1
Euro OTC	Dimeticone ointment 10% SR	3B180214	2
PKH Halle	Dimeticone ointment 10% SR	1A310118	1

- 8565 spectra from 734 *Apo-Ident* customers from a total of 3517 batches from a further 149 sub-

stances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dimeticone ointment 10% SR / Optiderm® lotion* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 235
Type B	0	100	0	20 701
Type C	0	35	0	8565

The substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.7778 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7866 %)	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 *Dimeticone ointment 10% SR / Optiderm® lotion* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
DMS® base cream classic	10.88	–
Hans Karrer Lipolotion MicroSilver	12.92	–
Asche Basis® lotion	17.92	–
Eucerinum W/O basis	20.07	–
Abitima® clinic face cream	20.33	–
Base cream Taoasis	26.31	–
Dexeryl®	28.42	–
DMS® base cream high classic	28.69	–
Excipial® U10 Lipolotio	29.06	–
La Roche-Posay Toleriane	29.36	–
Excipial® U Lipolotio	30.35	–

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Substanz	Distance in main model	Distance in second-stage model
Neribas® cream	31.48	–
Eucerinum O/W basis	36.16	–
Neuroderm® moisturising cream	38.28	–
Abitima® clinic body cream	39.02	–
Asche Basis® cream	39.93	–
Fabitop® base cream	41.61	–
DMS® base cream high classic plus	45.03	–
Amciderm® Base cream	47.37	–
Hans Karrer Lipocream MicroSilver	47.63	–
Dermatop® base cream	47.64	–
Linola® body milk	49.23	–
Allergika® Base cream	50.01	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dimeticone ointment 10% SR / Optiderm® lotion* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33268	33268	0.00	13.57
31759	31759	0.00	10.88
31266	31266	0.00	17.40
31243	31243	0.00	20.64
31638	31638	0.00	20.52
33041	33041	0.00	19.17

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 2.3-2021-01

Validated substance/substance group	**Dwarf pine oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31542-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Dwarf pine oil; Oleum pini pumilionis

Special notes

When selecting the *Dwarf pine oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Dwarf pine oil	4	3	6

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Dwarf pine oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Dwarf pine oil	586-116867	31542	60	not required
Taoasis	Dwarf pine oil	25599-120877	31689	60	not required
Taoasis	Dwarf pine oil	8783-127273	32937	40	not required
Taoasis	Dwarf pine oil	11148-1980	34109	40	not required

Validation samples

A total of 53 906 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 *Dwarf pine oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Dwarf pine oil*.
- 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
Primavera	Dwarf pine oil	00386M26	34377	40
Taoasis	Dwarf pine oil	8783-125163	32811	40
Taoasis	Dwarf pine oil	13260-3453	34290	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 batches from the substance/substance group *Dwarf pine oil*.
- 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
Taoasis	Dwarf pine oil	6635-122703	1
Taoasis	Dwarf pine oil	8238-124968	1
Taoasis	Dwarf pine oil	8783-125163	5
Taoasis	Dwarf pine oil	8238-126318	1
Taoasis	Dwarf pine oil	8783-127332	2
Taoasis/Taoasis	Dwarf pine oil	25599120877	1
Taoasis	Dwarf pine oil	11148-1980	1

- 8588 spectra from 736 *Apo-Ident* customers from a total of 3539 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Dwarf pine oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Dwarf pine oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	104	16	20 681
Type C	0	9	3	8588

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9455 %)	86.6667 % (> 84.1667 %)
Type C	100.0000 % (> 98.7902 %)	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 *Dwarf pine oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Spearmint oil	20.51	–
Angelica root oil	21.47	–
Swiss pine oil	34.12	–
Spruce needle oil	36.43	–
Juniper oil	38.59	–
Silver fir oil	43.99	–
Pine silvestris oil	44.12	–
Ginger oil	45.34	–
Citus oil	48.47	–
Citric oil	52.57	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31542	31542	0.00	29.51
31689	31689	0.00	29.91
32937	32937	0.00	21.47
34109	34109	0.00	29.59

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 2.3-2021-01

Validated substance/substance group	**Ethanol 70% pure / denatured**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30779-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ethanol 70% pure / denatured; Ethanolum 70% rein / vergällt

Special notes

When selecting the *Ethanol 70% pure / denatured* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ethanol 70% pure / denatured	4	3	341

Second-stage model

For differentiation of the substance/substance group *Ethanol 70% pure / denatured* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ethanol 70% pure / denatured*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
apomix	Ethanol 70% pure…	54A170613	31055	40	not required
apomix	Ethanol 70% pure…	08A060618	34274	40	not required
Hofmann's	Ethanol 70% pure…	271012	30779	80	1402563
Kremer GmbH &…	Ethanol 70% pure…	171211	34101	40	not required

Validation samples

A total of 53 906 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 *Ethanol 70% pure / denatured*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.

- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ethanol 70% pure / denatured*.

- 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
apomix	Ethanol 70% pure / denatured	01A020117	33217	40
Hofmann's	Ethanol 70% pure / denatured	570916	32591	40
Hofmann's	Ethanol 70% pure / denatured	750718	34317	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 461 spectra from 143 *Apo-Ident* customers from 349 batches from the substance/substance group *Ethanol 70% pure / denatured*.

- Among them are spectra of independent samples from 338 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
— (Retest)	Ethanol 70% pure / denatured	181009	1
A. Pflüger GmbH & Co. KG	Ethanol 70% pure / denatured	150209	1
A. Pflüger GmbH & Co. KG	Ethanol 70% pure / denatured	141127	1
A. Pflüger/Jenne	Ethanol 70% pure / denatured	131108	1
A. Pflüger/Phönix	Ethanol 70% pure / denatured	130607	1
A. Pflüger/Phönix	Ethanol 70% pure / denatured	130729	1
A.Pflüger	Ethanol 70% pure / denatured	21111301	1
A.Pflüger GmbH	Ethanol 70% pure / denatured	150730	1
A.Pflüger GmbH & Co.KG/...	Ethanol 70% pure / denatured	130514	1
A.Pflüger GmbH & Co.KG/...	Ethanol 70% pure / denatured	131011	1
A.Pflüger/Noweda	Ethanol 70% pure / denatured	130116	1
AHD	Ethanol 70% pure / denatured	170906	1
Caelo	Ethanol 70% pure / denatured	7028121	1
Alte Apo Defektur	Ethanol 70% pure / denatured	3019M-02320	1
Alte Apo Defektur	Ethanol 70% pure / denatured	1220E-02320	1
Anzag	Ethanol 70% pure / denatured	7027102	1
Anzag	Ethanol 70% pure / denatured	7028041	3
Anzag/ Otto Fischar Gmb...	Ethanol 70% pure / denatured	7024051	1
apomix	Ethanol 70% pure / denatured	77A310815	1
apomix	Ethanol 70% pure / denatured	15a170918	1
Apomix	Ethanol 70% pure / denatured	6A040213	1
apomix / Alliance Healt...	Ethanol 70% pure / denatured	3A140119	1
Apomix / Alliance Healt...	Ethanol 70% pure / denatured	37A110416	1
Apomix / Phönix	Ethanol 70% pure / denatured	41A180515	1
Apomix/Alliance Healthc...	Ethanol 70% pure / denatured	15A170215	1
Apomix/Alliance Healthc...	Ethanol 70% pure / denatured	56a020715	1
Apomix/Alliance Healthc...	Ethanol 70% pure / denatured	14A310718	1
Apomix/Noweda	Ethanol 70% pure / denatured	58A020715	1
apomix/Phoenix	Ethanol 70% pure / denatured	12A250116	1
Apotärze	Ethanol 70% pure / denatured	2015I-02320	1
Apotheke	Ethanol 70% pure / denatured	70105/51Dre	1
Apotheke	Ethanol 70% pure / denatured	70206/53Dre	1
Apotheke	Ethanol 70% pure / denatured	190723003	1
Apotheke im Forum	Ethanol 70% pure / denatured	150707	1
Apotheke im Forum	Ethanol 70% pure / denatured	300517	1

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Supplier	Substance	Batch	Spectra
Bahnhof-Apothek/Bahnhof...	Ethanol 70% pure / denatured	3819A-03043	1
Belous	Ethanol 70% pure / denatured	4613E-02320	1
Berkel AHK	Ethanol 70% pure / denatured	20042012397	1
Berkel AHK/HWA	Ethanol 70% pure / denatured	1410T31040613/70	1
Bombastus	Ethanol 70% pure / denatured	150630	1
Brennerei Gauß	Ethanol 70% pure / denatured	MLOG103/20	1
Brennerei Gauß	Ethanol 70% pure / denatured	MLOG505/2020	1
Brennerei Gauß	Ethanol 70% pure / denatured	MLOG604/2020	1
Brinn- Holtz	Ethanol 70% pure / denatured	1234-04/18	1
Brinn- Holtz	Ethanol 70% pure / denatured	1257-06/17	1
Caelo	Ethanol 70% pure / denatured	150730	1
Caelo	Ethanol 70% pure / denatured	46A120617	1
Caelo	Ethanol 70% pure / denatured	3A070918	1
Caelo	Ethanol 70% pure / denatured	7028041	1
Caelo	Ethanol 70% pure / denatured	814E-02320	1
Caelo	Ethanol 70% pure / denatured	20140403	1
Caelo	Ethanol 70% pure / denatured	2614E-03043	1
Caelo	Ethanol 70% pure / denatured	1715E-02320	1
Caelo	Ethanol 70% pure / denatured	19151-02320	1
Caelo	Ethanol 70% pure / denatured	151008	2
Caelo	Ethanol 70% pure / denatured	720318	1
Caelo	Ethanol 70% pure / denatured	3306	1
Caelo	Ethanol 70% pure / denatured	60307/50La	1
Caelo	Ethanol 70% pure / denatured	171211	1
Caelo	Ethanol 70% pure / denatured	7028111	1
Caelo	Ethanol 70% pure / denatured	7025081	1
Claudia Lange	Ethanol 70% pure / denatured	1234	1
Claudia Lange	Ethanol 70% pure / denatured	61010/51La	1
Claudia Lange	Ethanol 70% pure / denatured	60919/50La	1
Claudia Lange	Ethanol 70% pure / denatured	61107/50La	1
Defektur	Ethanol 70% pure / denatured	50427/52Wlo	1
Defektur	Ethanol 70% pure / denatured	50427/1La	1
Defektur	Ethanol 70% pure / denatured	2015Q-03043	1
Defektur	Ethanol 70% pure / denatured	60209/51Hk	1
Defektur	Ethanol 70% pure / denatured	1716M-03043	1
Defektur	Ethanol 70% pure / denatured	2517A-07097	1
Defektur	Ethanol 70% pure / denatured	2617I-07097	1
Defektur	Ethanol 70% pure / denatured	3317M-03043	1
Defektur	Ethanol 70% pure / denatured	71016/51Dre	1
Defektur	Ethanol 70% pure / denatured	80316/51Gie	1
Defektur	Ethanol 70% pure / denatured	80321/50Hk	1
Defektur	Ethanol 70% pure / denatured	80611/51Dre	1
Defektur	Ethanol 70% pure / denatured	3098	1
Defektur	Ethanol 70% pure / denatured	4712M-02320	1
Defektur	Ethanol 70% pure / denatured	270613EtOH	1
Defektur	Ethanol 70% pure / denatured	200114EtOH70	1
Defektur	Ethanol 70% pure / denatured	23/14	1
Defektur	Ethanol 70% pure / denatured	4714E-03043	1
Defektur / Wolf-Apotheke	Ethanol 70% pure / denatured	60902/50Hk	1
Defektur 10.06.2013	Ethanol 70% pure / denatured	2013-06-10Defektur	1
Defektur 20.01.2014	Ethanol 70% pure / denatured	2014-01-20B	1
Defektur Apotheke	Ethanol 70% pure / denatured	819I-03043	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	50714/51Hk	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	50714/53Hk	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	1234567	2
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	70227/52Dre	1
Defektur/Wolf-Apotheke	Ethanol 70% pure / denatured	41211/51Hk	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150114010	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150126002	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150219007	1

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Supplier	Substance	Batch	Spectra
Doppeleiche Apotheke	Ethanol 70% pure / denatured	150504003	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	190219005	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	200806002	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	200901002	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	201021001	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	3013A-02320	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	131227003	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140303003	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140630003	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	140927002	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	141029011	1
Doppeleiche Apotheke	Ethanol 70% pure / denatured	141208001	1
Dreikönigen Apotheke	Ethanol 70% pure / denatured	16049021	1
Eigen	Ethanol 70% pure / denatured	616Q-03043	2
Eigen	Ethanol 70% pure / denatured	3216E-03043	1
Eigen	Ethanol 70% pure / denatured	5016E-03043	1
Eigen	Ethanol 70% pure / denatured	Eigen	1
Eigen	Ethanol 70% pure / denatured	2419E-02320	1
Eigen	Ethanol 70% pure / denatured	620A-02320	1
EIGEN	Ethanol 70% pure / denatured	4117I-03043	1
EIGEN	Ethanol 70% pure / denatured	2118I-03043	1
EIGEN	Ethanol 70% pure / denatured	5218M-03043	1
Eigen/Defektur	Ethanol 70% pure / denatured	1116E-03043	1
Eigen/Defektur	Ethanol 70% pure / denatured	2516M-03043	1
Eigen/Defektur	Ethanol 70% pure / denatured	2716M-03043	1
Eigen/Defektur	Ethanol 70% pure / denatured	3416E-03043	1
eigene	Ethanol 70% pure / denatured	1018E-02320	1
eigene	Ethanol 70% pure / denatured	219I-02320	1
eigene	Ethanol 70% pure / denatured	2619E-02320	1
eigene herstellung	Ethanol 70% pure / denatured	SPV7026	1
eigene Herstellung	Ethanol 70% pure / denatured	6180115	1
eigene Herstellung	Ethanol 70% pure / denatured	4315Q-07016	1
eigene Herstellung	Ethanol 70% pure / denatured	317E-02320	1
eigene Herstellung	Ethanol 70% pure / denatured	1712904-A	1
eigene Herstellung	Ethanol 70% pure / denatured	4819I-03043	1
eigene Herstellung	Ethanol 70% pure / denatured	4411312106	1
eigene Herstellung	Ethanol 70% pure / denatured	431140218	1
Eigene Herstellung	Ethanol 70% pure / denatured	3618I-02320	1
Eigene Herstellung	Ethanol 70% pure / denatured	2919E-02320	1
Eigene Herstellung	Ethanol 70% pure / denatured	SPV7025	1
Eigene Herstellung	Ethanol 70% pure / denatured	SP70140	1
Eigene Herstellung	Ethanol 70% pure / denatured	SPV7029	1
Eigenherstellung	Ethanol 70% pure / denatured	5214A-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	1515I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	2015E-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4215l-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4615	1
Eigenherstellung	Ethanol 70% pure / denatured	4715M	1
Eigenherstellung	Ethanol 70% pure / denatured	616Q-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	2216A-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	3416E-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	517Q-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	170828001	1
Eigenherstellung	Ethanol 70% pure / denatured	5318A-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	14032019-01	1
Eigenherstellung	Ethanol 70% pure / denatured	Eigenherstellung	1
Eigenherstellung	Ethanol 70% pure / denatured	200715-01	1
Eigenherstellung	Ethanol 70% pure / denatured	1823	1
Eigenherstellung	Ethanol 70% pure / denatured	1313I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	2613I-03043	1

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Supplier	Substance	Batch	Spectra
Eigenherstellung	Ethanol 70% pure / denatured	2753	1
Eigenherstellung	Ethanol 70% pure / denatured	3413I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4513I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4733	1
Eigenherstellung	Ethanol 70% pure / denatured	5131213	1
Eigenherstellung	Ethanol 70% pure / denatured	2124	1
Eigenherstellung	Ethanol 70% pure / denatured	2314I-02320	1
Eigenherstellung	Ethanol 70% pure / denatured	4414A-02320	1
Eigenherstellung-Biozid	Ethanol 70% pure / denatured	FP200430-04	1
Eigenproduktion	Ethanol 70% pure / denatured	714Q-02320	1
Engel/Engel	Ethanol 70% pure / denatured	39-28715	1
Engel-Apotheke	Ethanol 70% pure / denatured	2319A-07016	1
Euro OTC	Ethanol 70% pure / denatured	77A110917	1
Euro OTC	Ethanol 70% pure / denatured	7028031	2
Euro OTC	Ethanol 70% pure / denatured	15A170918	1
Euro OTC	Ethanol 70% pure / denatured	220713	1
Fagron	Ethanol 70% pure / denatured	7027102	1
Fagron	Ethanol 70% pure / denatured	Probemessung	1
Fagron	Ethanol 70% pure / denatured	40929/52La	1
Fiebig	Ethanol 70% pure / denatured	7029051	1
Fischar	Ethanol 70% pure / denatured	27031501	1
Fischar	Ethanol 70% pure / denatured	7025082	1
Fischar	Ethanol 70% pure / denatured	7028031	1
Fischar	Ethanol 70% pure / denatured	7028011	1
Fischar	Ethanol 70% pure / denatured	7028062	1
Fischar	Ethanol 70% pure / denatured	7028041	1
Fischar	Ethanol 70% pure / denatured	7029082	1
Fischar	Ethanol 70% pure / denatured	7029101	1
Fischar	Ethanol 70% pure / denatured	7020046	1
Fischar	Ethanol 70% pure / denatured	7024051	1
Fischar / Alliance Hea…	Ethanol 70% pure / denatured	7026051	1
Fischar / Alliance Hea…	Ethanol 70% pure / denatured	7028102	1
Fischar / Alliance Hea…	Ethanol 70% pure / denatured	7029041	1
Fischar / Anzag	Ethanol 70% pure / denatured	7023091	1
Fischar / Noweda	Ethanol 70% pure / denatured	7023111	1
Fischar / Noweda	Ethanol 70% pure / denatured	7024021	1
Fischar / Sanacorp	Ethanol 70% pure / denatured	7023091	1
Fischar GmbH	Ethanol 70% pure / denatured	7028062	1
Fischar/Phoenix	Ethanol 70% pure / denatured	7029102	1
Fischar/Phoenix	Ethanol 70% pure / denatured	7028081	1
fischar/Phönix	Ethanol 70% pure / denatured	7027032	1
Fischar/Phönix	Ethanol 70% pure / denatured	7026031	1
Fischar/Phönix	Ethanol 70% pure / denatured	7026092	1
Fischar/Phönix	Ethanol 70% pure / denatured	7026111	1
Fischar/Phönix	Ethanol 70% pure / denatured	7027031	2
Fischar/Phönix	Ethanol 70% pure / denatured	7028102	1
Fischar/Sanacorp	Ethanol 70% pure / denatured	7028031	1
Fischar/Sanacorp	Ethanol 70% pure / denatured	7027102	1
Fischar/Sanacorp	Ethanol 70% pure / denatured	7028062	1
Fischar/Sanacorp	Ethanol 70% pure / denatured	7028081	1
Fischer	Ethanol 70% pure / denatured	7028111	1
fishar	Ethanol 70% pure / denatured	7028111	1
Gehe	Ethanol 70% pure / denatured	3818Q-02320	1
GEHE	Ethanol 70% pure / denatured	180828	1
Gehe 27.2.14	Ethanol 70% pure / denatured	140121	1
Gehe/Pflüger	Ethanol 70% pure / denatured	1204021712	1
Gehe/Pflüger	Ethanol 70% pure / denatured	160909	2
Gehe/Pflüger	Ethanol 70% pure / denatured	170308	1
Gehe/Pflüger	Ethanol 70% pure / denatured	170208	1
Gehe/Pflüger	Ethanol 70% pure / denatured	170419	2

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Supplier	Substance	Batch	Spectra
Gehe/Pflüger	Ethanol 70% pure / denatured	180928	1
Gehe/PKH	Ethanol 70% pure / denatured	28A300420	1
Gehe-Kremer	Ethanol 70% pure / denatured	150209	1
Gehe-Kremer	Ethanol 70% pure / denatured	140307	1
Gersprenz Apo	Ethanol 70% pure / denatured	3519A-02320	1
Goethe Apotheke	Ethanol 70% pure / denatured	RD201026-0002	1
Goetheapotheke	Ethanol 70% pure / denatured	3820E-03043	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	3412I-03043	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	130502003	1
Gutenberg-Apotheke	Ethanol 70% pure / denatured	1813M-02320	1
Heck/Wittich	Ethanol 70% pure / denatured	2113N-02320	1
Hetterich - Teofarma sr...	Ethanol 70% pure / denatured	145501/R	2
Hetterich - Teofarma sr...	Ethanol 70% pure / denatured	145601	3
Hetterich/ Noweda	Ethanol 70% pure / denatured	145703	1
Hetterich/ Noweda	Ethanol 70% pure / denatured	1801T	1
Hetterich/ Noweda	Ethanol 70% pure / denatured	145802	1
Hetterich/ Sanacorp	Ethanol 70% pure / denatured	145703	1
Hetterich/AEP	Ethanol 70% pure / denatured	145802	1
Hetterich/AHCA	Ethanol 70% pure / denatured	145703	2
Hetterich/Ebert	Ethanol 70% pure / denatured	145401	2
Hirsch	Ethanol 70% pure / denatured	4413I-02320	1
Hirsch	Ethanol 70% pure / denatured	714E-02320	1
HirschApotheke	Ethanol 70% pure / denatured	10151-02320	1
HirschApotheke	Ethanol 70% pure / denatured	2315I-02320	1
HirschApotheke	Ethanol 70% pure / denatured	4614A-02320	1
Hoffmann & Sommer	Ethanol 70% pure / denatured	750718	1
Hoffmann & Sommer GmbH ...	Ethanol 70% pure / denatured	580916	1
Hoffmann & Sommer GmbH ...	Ethanol 70% pure / denatured	650917	1
Hoffmanns/Anzag	Ethanol 70% pure / denatured	520116	1
Hofman und Sommer GmbH ...	Ethanol 70% pure / denatured	580916	1
Hofmann	Ethanol 70% pure / denatured	320713	1
Hofmann & Sommer	Ethanol 70% pure / denatured	691217	1
Hofmann /Phoenix	Ethanol 70% pure / denatured	900320	1
Hofmann u. Sommer	Ethanol 70% pure / denatured	720318	1
Hofmann&Sommer/Sanacorp	Ethanol 70% pure / denatured	781218	1
Hofmann's	Ethanol 70% pure / denatured	940420	1
Hohe-Wart-Apotheke	Ethanol 70% pure / denatured	23072013/1	1
Hubertus Apotheke	Ethanol 70% pure / denatured	261113	1
Kastner (eigen)	Ethanol 70% pure / denatured	1215E-02320	1
Kastner (eigen)	Ethanol 70% pure / denatured	3114E-03043	1
Kemer Phönix	Ethanol 70% pure / denatured	130628	1
Klenk	Ethanol 70% pure / denatured	150730	1
Kremer	Ethanol 70% pure / denatured	160909	1
Kremer	Ethanol 70% pure / denatured	160711	1
Kremer	Ethanol 70% pure / denatured	170308	1
Kremer	Ethanol 70% pure / denatured	170619	1
Kremer	Ethanol 70% pure / denatured	180404	1
Kremer	Ethanol 70% pure / denatured	180828	2
Kremer	Ethanol 70% pure / denatured	181206	1
Kremer	Ethanol 70% pure / denatured	130206	1
Kremer	Ethanol 70% pure / denatured	141027	1
Kremer	Ethanol 70% pure / denatured	160414	1
Kremer	Ethanol 70% pure / denatured	161017	1
Kremer	Ethanol 70% pure / denatured	170208	1
kremer gmbh	Ethanol 70% pure / denatured	23081605	1
Kremer GmbH	Ethanol 70% pure / denatured	160512	1
Kremer GmbH	Ethanol 70% pure / denatured	170906	1
Kremer GmbH	Ethanol 70% pure / denatured	181206	1
Kremer GmbH & Co.KG	Ethanol 70% pure / denatured	140902	2
Kremer GmbH & Co.KG	Ethanol 70% pure / denatured	150602	1

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Supplier	Substance	Batch	Spectra
Kremer GmbH &Co. KG	Ethanol 70% pure / denatured	160215	1
Kremer GmbH &Co. KG	Ethanol 70% pure / denatured	170208	1
Kremer GmbH &Co. KG	Ethanol 70% pure / denatured	161017	1
Kremer GmbH &Co. KG	Ethanol 70% pure / denatured	170116	2
Kremer GmbH &Co. KG	Ethanol 70% pure / denatured	170619	4
Kremer Gmbh / Noweda	Ethanol 70% pure / denatured	141127	2
Kremer Gmbh / Noweda	Ethanol 70% pure / denatured	140627	1
Kremer GmbH Wuppertal/G...	Ethanol 70% pure / denatured	130729	1
Kremer GmbH/Noweda	Ethanol 70% pure / denatured	181115	1
Kremer GmbH/Phönix	Ethanol 70% pure / denatured	150327	1
Kremer/Alliance Healthc...	Ethanol 70% pure / denatured	171025	1
Kremer/Gehe	Ethanol 70% pure / denatured	160414	2
Kremer/Gehe	Ethanol 70% pure / denatured	130116	1
Kremer/Gehe	Ethanol 70% pure / denatured	140121	1
Kremer/Noweda	Ethanol 70% pure / denatured	170906	1
Kremer/Noweda	Ethanol 70% pure / denatured	131011	1
Kremer/Phoenix	Ethanol 70% pure / denatured	150730	1
Kremer/Phönix	Ethanol 70% pure / denatured	150327	1
Kremer/Phönix	Ethanol 70% pure / denatured	151123	1
Kremer/Phönix	Ethanol 70% pure / denatured	180404	1
Kremer/Phönix	Ethanol 70% pure / denatured	180928	1
Kremer/Phönix	Ethanol 70% pure / denatured	190321	1
Kremer/Phönix	Ethanol 70% pure / denatured	141127	1
KremperGmbH & Co. KG	Ethanol 70% pure / denatured	140507	1
kruppa	Ethanol 70% pure / denatured	1216H4	1
kruppa	Ethanol 70% pure / denatured	617H4	1
Kruppa	Ethanol 70% pure / denatured	418H2	1
Kruppa	Ethanol 70% pure / denatured	818H2	1
Lamotte/AHCA	Ethanol 70% pure / denatured	6007153001	1
Lamotte/AHCA	Ethanol 70% pure / denatured	6010634001	4
Libellen Apotheke	Ethanol 70% pure / denatured	1515Q-02320	1
Löwen-Apotheke	Ethanol 70% pure / denatured	219Q-03043	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-121214-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-050515-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-110716-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-021116-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	A-311013-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	A-061213-3D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-100114-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-020314-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-080514-1D	1
Martinus-Apotheke	Ethanol 70% pure / denatured	E-180714-1D	1
Met/ Noweda	Ethanol 70% pure / denatured	3815M-03043	1
n.a.	Ethanol 70% pure / denatured	1707918-a	1
Noweda	Ethanol 70% pure / denatured	120420	1
Noweda/KremerGmbH	Ethanol 70% pure / denatured	130821	1
Noweda/Pflüger	Ethanol 70% pure / denatured	190606	1
O:Fischar/Phönix	Ethanol 70% pure / denatured	7027032	1
Otto Fischar	Ethanol 70% pure / denatured	7028121	1
Otto Fischar	Ethanol 70% pure / denatured	7023111	1
Otto Fischar GmbH & Co....	Ethanol 70% pure / denatured	7025031	2
Otto Fischar GmbH & Co....	Ethanol 70% pure / denatured	7028041	1
Otto Fischar GmbH & Co....	Ethanol 70% pure / denatured	7024021	1
Otto Fischar GmbH & Co....	Ethanol 70% pure / denatured	7024071	1
Otto Fischar GmbH/ Amzag	Ethanol 70% pure / denatured	7024091	1
Otto Fischar/ Anzag	Ethanol 70% pure / denatured	7029021	1
Otto Fischer / Noweda	Ethanol 70% pure / denatured	7025031	1
Otto Fischer GmbH & Co....	Ethanol 70% pure / denatured	7029121	1
Otto Fischer GmbH&Co.KG...	Ethanol 70% pure / denatured	7028091	1
Otto Fischer/ Noweda	Ethanol 70% pure / denatured	7029051	1

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Supplier	Substance	Batch	Spectra
otto Fischer/Noweda	Ethanol 70% pure / denatured	7024121	1
Otto/Fischer	Ethanol 70% pure / denatured	1029051	1
Pflüger	Ethanol 70% pure / denatured	170906	1
Pflüger	Ethanol 70% pure / denatured	171025	1
Pflüger	Ethanol 70% pure / denatured	180308	1
Pflüger	Ethanol 70% pure / denatured	190430	2
Pflüger	Ethanol 70% pure / denatured	190606	1
Pflüger	Ethanol 70% pure / denatured	200302	1
Pflüger	Ethanol 70% pure / denatured	200311	2
Pflüger	Ethanol 70% pure / denatured	130607	1
Pflüger	Ethanol 70% pure / denatured	131108	2
Pflüger	Ethanol 70% pure / denatured	141027	1
Pflüger GmbH & Co.KG	Ethanol 70% pure / denatured	170116	1
Pflüger GmbH / Gehe	Ethanol 70% pure / denatured	180404	1
Pflüger/ Noweda	Ethanol 70% pure / denatured	180404	1
Pflüger/Gehe	Ethanol 70% pure / denatured	170619	1
Pflüger/Gehe	Ethanol 70% pure / denatured	200313	1
Pflüger/Phönix	Ethanol 70% pure / denatured	190430	1
Pflüger/Phönix	Ethanol 70% pure / denatured	200319	1
Phoenix	Ethanol 70% pure / denatured	7027032	1
Phoenix	Ethanol 70% pure / denatured	7027103	1
Phoenix	Ethanol 70% pure / denatured	7029082	1
Phönix	Ethanol 70% pure / denatured	351213	1
PHÖNIX	Ethanol 70% pure / denatured	171025	1
PHÖNIX	Ethanol 70% pure / denatured	171211	1
Caelo	Ethanol 70% pure / denatured	7023111	1
Euro OTC	Ethanol 70% pure / denatured	170116	1
Phönix/Kremer	Ethanol 70% pure / denatured	160711	1
Phönix/Kremer	Ethanol 70% pure / denatured	180525	1
Phönix/Otto Fischar	Ethanol 70% pure / denatured	7029082	1
Plüger/Anzag	Ethanol 70% pure / denatured	32016	1
Post-Apotheke	Ethanol 70% pure / denatured	1414A-02320	1
Post-Apotheke 15.01.2014	Ethanol 70% pure / denatured	15012044	1
Purren Apotheke	Ethanol 70% pure / denatured	17043	1
Rezeptur	Ethanol 70% pure / denatured	4215Q-03043	1
Rezeptur Apotheke	Ethanol 70% pure / denatured	2016Q-03043	1
Rezeptur Apotheke	Ethanol 70% pure / denatured	917Q-03043	1
Römer-Apotheke	Ethanol 70% pure / denatured	4314A-03043	1
Rondell	Ethanol 70% pure / denatured	1715E-07145	1
Rondell Apotheke	Ethanol 70% pure / denatured	26151-07145	1
Rondell Apotheke	Ethanol 70% pure / denatured	4015A-03043	1
Rondell Apotheke	Ethanol 70% pure / denatured	416M-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	415M-03043	1
Rondell Apotheke	Ethanol 70% pure / denatured	2616M-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	1814Q-07145	1
Rondell Apotheke	Ethanol 70% pure / denatured	3414M-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	3414M-07145	1
Rondell Apotheke	Ethanol 70% pure / denatured	615E-02320	1
Rondell Apotheke	Ethanol 70% pure / denatured	615E-07145	1
Rosen Apotheke	Ethanol 70% pure / denatured	1317A-07095	1
Rosenapotheke	Ethanol 70% pure / denatured	2317E-07095	1
Sanacorp	Ethanol 70% pure / denatured	7028081	3
Sanacorp	Ethanol 70% pure / denatured	130124	1
Sanacorp/Pflüger	Ethanol 70% pure / denatured	170906	1
sittig	Ethanol 70% pure / denatured	310316	1
Stadt-Apo	Ethanol 70% pure / denatured	5018A-03043	2
Stern-Defektur	Ethanol 70% pure / denatured	130705003	1
Stiftsapotheke	Ethanol 70% pure / denatured	150420005	1
Stiftsapotheke	Ethanol 70% pure / denatured	13052016	1
Töste Apotheke	Ethanol 70% pure / denatured	319E-03043	1

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Supplier	Substance	Batch	Spectra
Töste Apotheke	Ethanol 70% pure / denatured	1119A-03043	1
Töste Apotheke	Ethanol 70% pure / denatured	2919A-03043	1
Töste Apotheke	Ethanol 70% pure / denatured	4819A-03043	1
Töste Apotheke	Ethanol 70% pure / denatured	2520A-03043	1
Vita Apotheke	Ethanol 70% pure / denatured	190531006	1
VitaFit	Ethanol 70% pure / denatured	2020-04-17	2
VWR Chemicals	Ethanol 70% pure / denatured	20b254009	1
VWR Chemicals	Ethanol 70% pure / denatured	20B254009	1
Wolf Apotheke/Defektur	Ethanol 70% pure / denatured	70627/52Hk	1
Wolf Apotheke/Defektur	Ethanol 70% pure / denatured	71208/50Gie	1
Wolf-Apotheke	Ethanol 70% pure / denatured	40331/52La	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	51019/51Wlo	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	Bulk	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	70404/53Hk	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	40722/51Hk	1
Wolf-Apotheke / Defektur	Ethanol 70% pure / denatured	41125/52Hk	1
Wolf-Apotheke-Defektur	Ethanol 70% pure / denatured	70818/50Hk	1
Apotheke	Ethanol 70% pure / denatured		1
Berkel AHK	Ethanol 70% pure / denatured		1
Brennerei Gauß	Ethanol 70% pure / denatured		1
Caelo	Ethanol 70% pure / denatured		1
Defektur	Ethanol 70% pure / denatured		2
Die LindenApotheke / Bl...	Ethanol 70% pure / denatured		1
Direktlieferung	Ethanol 70% pure / denatured		1
eigen	Ethanol 70% pure / denatured		2
Eigenherstellung	Ethanol 70% pure / denatured		1
frischhergestellt	Ethanol 70% pure / denatured		1
	Ethanol 70% pure / denatured		1
Nachprüfung	Ethanol 70% pure / denatured		1
Wolf Apotheke	Ethanol 70% pure / denatured		2

- 8139 spectra from 725 *Apo-Ident* customers from a total of 3198 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ethanol 70% pure / denatured* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ethanol 70% pure / denatured* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	120	0	20 681
Type C	0	442	19	8139

The substance/substance group *Ethanol 70% pure / denatured* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7849 %)	95.8785 % (> 95.2278 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ethanol 70% pure / denatured* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Orange aroma	54.85	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ethanol 70% pure / denatured* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30779	30779	0.00	101.19
34101	34101	0.00	95.58
31055	31055	0.00	83.05
34274	34274	0.00	82.09

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 2.3-2021-01

Validated substance/substance group	**Excipial® almond oil ointment**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30720-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Excipial® almond oil ointment

Special notes

When selecting the *Excipial® almond oil ointment* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Excipial® almond oil ointment	4	2	34

Second-stage model

For differentiation of the substance/substance group *Excipial® almond oil ointment* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Excipial® almond oil ointment*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Spirig Pharma	Excipial® almond…	M023	30720	40	not required
Spirig Pharma	Excipial® almond…	M031	31090	40	not required
Spirig Pharma	Excipial® almond…	N012	31278	40	not required
Spirig Pharma	Excipial® almond…	R012	31757	60	not required

Validation samples

A total of 53 906 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 *Excipial® almond oil ointment*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.

- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Excipial® almond oil ointment*.

- 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
Spirig Pharma	Excipial® almond oil ointment	S021	33209	40
Spirig Pharma	Excipial® almond oil ointment	T052	33210	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 19 *Apo-Ident* customers from 35 batches from the substance/substance group *Excipial® almond oil ointment*.

- 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	Excipial® almond oil ointment	lotno32	1
Caelo	Excipial® almond oil ointment	20170829Ma2	1
Caelo	Excipial® almond oil ointment	20170829Ma3	1
Ebert & Jacobi	Excipial® almond oil ointment	50239	1
Fiebig	Excipial® almond oil ointment	S051	1
Galderma	Excipial® almond oil ointment	R043	1
Galderma	Excipial® almond oil ointment	50498	1
Galderma	Excipial® almond oil ointment	8774004	1
Galderma (Spirig Pharma…	Excipial® almond oil ointment	R043	1
Galderma International …	Excipial® almond oil ointment	T031	1
Galderma/Alliance	Excipial® almond oil ointment	V061	1
Galderma/Anzag	Excipial® almond oil ointment	S033	1
Galderma/Kehr	Excipial® almond oil ointment	T051	1
Galderma/Kehr	Excipial® almond oil ointment	V031	1
Galderma/Now	Excipial® almond oil ointment	LOTS021	1
Galderma/Noweda	Excipial® almond oil ointment	S012	1
Galderma/Phönix	Excipial® almond oil ointment	R043	1
Galderma/Phönix	Excipial® almond oil ointment	S021	3
Galderma/Phönix	Excipial® almond oil ointment	50239	3
Galderma/Phönix	Excipial® almond oil ointment	9774002	1
Galderma/Phönix	Excipial® almond oil ointment	8774007	1
Galderma-Spirig	Excipial® almond oil ointment	V042-20171127Ma12	1
Noweda	Excipial® almond oil ointment	8774004	1
Noweda	Excipial® almond oil ointment	9774003	1
Noweda	Excipial® almond oil ointment	9774005	2
Phoenix	Excipial® almond oil ointment	LOTN022	2
Spirg	Excipial® almond oil ointment	M032	1
Spirig	Excipial® almond oil ointment	LOTM023	1
Spirig	Excipial® almond oil ointment	N031	1
Spirig	Excipial® almond oil ointment	N032	1
Spirig	Excipial® almond oil ointment	MO23	1
Spirig	Excipial® almond oil ointment	R012	1
Spirig	Excipial® almond oil ointment	S032	1
Spirig	Excipial® almond oil ointment	S011	1
Spirig / Galderma / Anzag	Excipial® almond oil ointment	V061	1
Spirig / Gehe	Excipial® almond oil ointment	LOTN022	1

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Supplier	Substance	Batch	Spectra
Spirig /Noweda	Excipial® almond oil ointment	R012	1
Spirig /Noweda	Excipial® almond oil ointment	r021	1
Spirig Pharma AG/Noweda	Excipial® almond oil ointment	50239	1
Spirig Pharma/Nowed	Excipial® almond oil ointment	NO22	1
Spirig/AHD	Excipial® almond oil ointment	N011	1
Spirig/Noweda	Excipial® almond oil ointment	R043	1
Spirig/Phönix	Excipial® almond oil ointment	N031	1
Spirig/Sanacorp	Excipial® almond oil ointment	LOTN011	1

- 8550 spectra from 736 *Apo-Ident* customers from a total of 3521 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Excipial® almond oil ointment* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Excipial® almond oil ointment* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	49	1	8550

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7861 %)	98.0000 % (> 92.0000 %)

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 *Excipial® almond oil ointment* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Balm Bio Nature	11.85	–
Argan oil	18.06	–
Wax ointment (stabilised)	43.17	–
White paraffin oil	54.25	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30720	30720	0.00	31.09
31278	31278	0.00	25.97
31090	31090	0.00	24.83
31757	31757	0.00	23.23

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 2.3-2021-01

Validated substance/substance group	**Fat ointments**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30881-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Fat ointments; Asche Basis® fat ointment; Cottonwood ointment; Deumavan® protection ointment neutral; Marjoram ointment; Neribas® fat ointment; Protegin® XN; Unguentum majoranae; Unguentum Populi

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Asche Basis® fat ointment	3	0	8
Cottonwood ointment	6	5	2
Deumavan® protection ointment neutral	2	1	0
Marjoram ointment	4	7	92
Neribas® fat ointment	3	2	8
Protegin® XN	3	1	77

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Fat ointments*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Chiesi	Asche Basis® fat…	23014A	31013	40	not required
Chiesi	Asche Basis® fat…	41017A	31858	60	not required
Chiesi	Asche Basis® fat…	53021A	33634	40	not required
Caelo	Cottonwood ointm…	161175	32473	40	20160607*
Caelo	Cottonwood ointm…	170572	33130	40	20170307*
Caelo	Cottonwood ointm…	170573	33131	40	20170308*
Caelo	Cottonwood ointm…	191253	34783	40	20190529*
Caelo	Cottonwood ointm…	20001373	34966	40	20200513*
Caelo	Cottonwood ointm…	20000881	34967	40	20200325*
Kaymogyn GmbH	Deumavan® protec…	41920120	35069	40	not required
Kaymogyn GmbH	Deumavan® protec…	13781119	35071	40	not required
Caelo	Marjoram ointment	12123001	30881	40	not required
Caelo	Marjoram ointment	14089901	31443	40	not required
Caelo	Marjoram ointment	20000281	34963	40	20200207*
Henry Lamotte	Marjoram ointment	5322500	30926	40	not required
Jenapharm	Neribas® fat oin…	32032C	31489	40	not required
Jenapharm	Neribas® fat oin…	YY00K7C	31872	60	not required
Jenapharm	Neribas® fat oin…	YY01TF2	33986	40	not required
Caelo	Protegin® XN	13081901	31112	40	not required
Caelo	Protegin® XN	13344402	31475	40	not required
Caelo	Protegin® XN	17258703	33921	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 880 spectra of 21 reference samples from the substance/substance group *Fat ointments*. These samples are listed above in the *calibration samples* section. The reference samples come from 21 different batches.

- 23 625 spectra from a total of 483 batches from further 155 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with

*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.

the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 760 spectra of 18 reference samples from the substance/substance group *Fat ointments*.
- Among them are spectra of independent samples from 16 batches from which no spectra 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	Cottonwood ointment	170534	33162	40
Caelo	Cottonwood ointment	170574	33163	40
Caelo	Cottonwood ointment	180826	34186	40
Caelo	Cottonwood ointment	180828	34187	40
Caelo	Cottonwood ointment	181888	34256	40
Kaymogyn GmbH	Deumavan® protection ointmen…	62170320	35070	40
Caelo	Marjoram ointment	153533	31990	60
Caelo	Marjoram ointment	153540	31991	60
Caelo	Marjoram ointment	160687	32516	40
Caelo	Marjoram ointment	162575	32872	40
Caelo	Marjoram ointment	162576	32873	40
Caelo	Marjoram ointment	181900	34259	40
Fagron	Marjoram ointment	18L18-T07-062832	34418	40
Jenapharm	Neribas® fat ointment	YY011K0	32764	40
Jenapharm	Neribas® fat ointment	YY019KR	33290	40
Caelo	Protegin® XN	161645	32340	40
Chiesi	Asche Basis® fat ointment	53021A	32716	40
Chiesi	Asche Basis® fat ointment	53021A	32925	40

- 20 041 spectra from a total of 430 batches from further 198 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 665 spectra from 227 *Apo-Ident* customers from 199 batches from the substance/substance group *Fat ointments*.
- Among them are spectra of independent samples from 186 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	Asche Basis® fat ointment	73025A	3
Chiese	Asche Basis® fat ointment	33016A	1
Chiese	Asche Basis® fat ointment	63023A	1
Chiesi	Asche Basis® fat ointment	51020A	1
Chiesi	Asche Basis® fat ointment	63023A	1
Chiesi	Asche Basis® fat ointment	84028A	1
Chiesi	Asche Basis® fat ointment	81026A	1
Chiesi	Asche Basis® fat ointment	82027A	1
CHiesi	Asche Basis® fat ointment	41018A	3
Chiesi/ Noweda	Asche Basis® fat ointment	82027A	1
Chiesi/Gehe	Asche Basis® fat ointment	51020A	1
Chiesi/Gehe	Asche Basis® fat ointment	41017A	1
Caelo	Cottonwood ointment	18019902	1
Jenne	Cottonwood ointment	17057404	1
Lamotte/ Noweda	Marjoram ointment	5322500	1
Caelo	Marjoram ointment	10111402	1
Caelo	Marjoram ointment	20000282001	1
Caelo	Marjoram ointment	11274603	2
Caelo	Marjoram ointment	11327501	2
Caelo	Marjoram ointment	11061201	1
Caelo	Marjoram ointment	12081002	5
Caelo	Marjoram ointment	15101205	1
Caelo	Marjoram ointment	12018001	4
Caelo	Marjoram ointment	12018101	3
Caelo	Marjoram ointment	7121203	1
Caelo	Marjoram ointment	20290312-1	1
Caelo	Marjoram ointment	5322500	1
Caelo	Marjoram ointment	8031304	1
Caelo	Marjoram ointment	13051304	1
Caelo	Marjoram ointment	13028401	9
Caelo	Marjoram ointment	2011405	1
Caelo	Marjoram ointment	13382902	1
Caelo	Marjoram ointment	140020101	1
Caelo	Marjoram ointment	14090002	10
Caelo	Marjoram ointment	2021506	1
Caelo	Marjoram ointment	15354001	5
Caelo	Marjoram ointment	27031505	1
Caelo	Marjoram ointment	312115354001	1
Caelo	Marjoram ointment	16068602	5
Caelo	Marjoram ointment	16257602	4
Caelo	Marjoram ointment	16257502	3
Caelo	Marjoram ointment	17071101	7
Caelo	Marjoram ointment	17302401	6
Caelo	Marjoram ointment	18190001	11
Caelo	Marjoram ointment	19033001	12
Caelo	Marjoram ointment	1903301	1
Caelo	Marjoram ointment	18251603	1
Caelo	Marjoram ointment	19033101	1
Caelo	Marjoram ointment	13382903	2
Caelo	Marjoram ointment	14332202	1
Caelo	Marjoram ointment	15392402	2
Caelo	Marjoram ointment	15038401	2
Caelo	Marjoram ointment	66(18050902)	1
Caelo	Marjoram ointment	66(18190001)	1
Caelo	Marjoram ointment	18D11-T01-054700	1
Caelo	Marjoram ointment	18190102	3
Caelo	Marjoram ointment	13028302	3
Caelo	Marjoram ointment	1225402	1
Caelo	Marjoram ointment	17071001	2
Caelo	Marjoram ointment	19115103	2

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Supplier	Substance	Batch	Spectra
Caelo	Marjoram ointment	15038501	3
Caelo	Marjoram ointment	65(17070901)	1
Caelo	Marjoram ointment	15038303	1
Caelo	Marjoram ointment	13095401	5
Caelo	Marjoram ointment	17070901	9
Caelo	Marjoram ointment	13383001	1
Caelo	Marjoram ointment	13e10-t04-003550	1
Caelo	Marjoram ointment	16068701	5
Caelo	Marjoram ointment	19033102	7
Caelo	Marjoram ointment	12295402	6
Caelo	Marjoram ointment	13307102	6
Caelo	Marjoram ointment	14332101	9
Caelo	Marjoram ointment	16068901	8
Caelo	Marjoram ointment	17302402	1
Caelo	Marjoram ointment	14002101	16
Caelo	Marjoram ointment	16068801	3
Caelo	Marjoram ointment	16K07-T20-038496	1
Caelo	Marjoram ointment	18050901	4
Caelo	Marjoram ointment	18190101	4
Caelo	Marjoram ointment	1513E-02536	1
Caeolo	Marjoram ointment	14090002	1
Caeolo	Marjoram ointment	1539402	1
Caesar & Lorenz Sanacorp	Marjoram ointment	19033102	1
Caesar & Loretz GmbH	Marjoram ointment	19033001	1
Caleo/ Noweda	Marjoram ointment	17302402	2
Caleo/ Noweda	Marjoram ointment	17302401	1
Cealo	Marjoram ointment	13028401	2
Fagron	Marjoram ointment	12d24-t01	1
Fagron	Marjoram ointment	12081002	1
Fagron	Marjoram ointment	12D24-T02	1
Fagron	Marjoram ointment	13A16-To4-000208	1
Fagron	Marjoram ointment	13a16-0001	1
Fagron	Marjoram ointment	13F27-T03-004962	3
Fagron	Marjoram ointment	13F27-To3-004962	2
Fagron	Marjoram ointment	16K07-T20-038496	4
Fagron	Marjoram ointment	17B03-T02-041256	2
Fagron	Marjoram ointment	17E22-T09-044517	2
Fagron	Marjoram ointment	18L18-T07-062832	4
Fagron	Marjoram ointment	15K10-T10-027644	3
Fagron	Marjoram ointment	18D11-T01-054700	1
Fagron	Marjoram ointment	14090002	1
Fagron	Marjoram ointment	16E02-T02-032846	1
Fagron	Marjoram ointment	13A16-T02	1
Fagron	Marjoram ointment	12D24-T01	2
Fagron	Marjoram ointment	13A16-T04-000208	1
Fagron	Marjoram ointment	14A07-T06-009085	3
Fagron	Marjoram ointment	14A07-T05-009082	2
Fagron	Marjoram ointment	14A07-T04-009079	3
Fagron	Marjoram ointment	18Dn-T01-054700	1
Fagron	Marjoram ointment	19G04-T03-069133	2
Fagron	Marjoram ointment	14a07-T04009079	1
Gehe	Marjoram ointment	13307102	1
Gehe	Marjoram ointment	14090002	1
Gehe	Marjoram ointment	15038501	1
Gehe	Marjoram ointment	15354001	1
Gehe	Marjoram ointment	16257602	2
Gehe	Marjoram ointment	17071001	1
Gehe	Marjoram ointment	19033001	1
Caelo	Marjoram ointment	12123101	2
Caelo	Marjoram ointment	13028301	2

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Supplier	Substance	Batch	Spectra
Caelo	Marjoram ointment	13382901	1
Henry Lamotte	Marjoram ointment	5563400	1
Henry Lamotte GmbH/Hold…	Marjoram ointment	5067400	1
Henry Lamotte Oils	Marjoram ointment	5067400	1
Henry Lamotte Oils GmbH	Marjoram ointment	5322500	1
Henry Lamotte Oils GmbH	Marjoram ointment	5563400	1
Henry Lamotte Oils GmbH…	Marjoram ointment	5067400	1
Henry Lamotte Oils GmbH…	Marjoram ointment	5322500	1
Jenne	Marjoram ointment	13028302	2
Kehr	Marjoram ointment	17071101	1
Lamotte / Gehe	Marjoram ointment	5322500	1
Lamotte/Alliance	Marjoram ointment	5563400	3
Lamotte/Sanacorp	Marjoram ointment	5563400	1
Noweda	Marjoram ointment	5322500	1
Caelo	Marjoram ointment	15353303	1
Caelo	Marjoram ointment	18050902	3
Phoenix	Marjoram ointment	13028401	1
Phönix	Marjoram ointment	12018001	1
Phönix	Marjoram ointment	16068901	1
Phönix	Marjoram ointment	17071001	1
Phönix	Marjoram ointment	17302401	1
Phönix	Marjoram ointment	18190001	2
Phönix 10.12.12	Marjoram ointment	12D24-T02	1
Sanacorp	Marjoram ointment	12081002	1
Sanacorp	Marjoram ointment	12295402	1
Sanacorp	Marjoram ointment	13095401	1
Sanacorp	Marjoram ointment	16257502	2
Sanacorp, 21.03.17, 5,73EUR	Marjoram ointment	16068602	1
Spangropharm	Marjoram ointment	4961000	1
VDL	Marjoram ointment	14090002	1
/ AHD	Neribas® fat ointment	YY016LP	2
Alliance Healthcare	Neribas® fat ointment	YY0431T	1
BAYER/Phönix WE:26.04.1…	Neribas® fat ointment	YY011K0	1
Caelo	Neribas® fat ointment	yy00k7C	1
GP Grenzach Produktions…	Neribas® fat ointment	YY00K7C	1
Hedinger/Sanacorp	Neribas® fat ointment	YY01TF2	2
Jenapharm	Neribas® fat ointment	YY0282F	1
Jenapharm / Fiebig	Neribas® fat ointment	YY01TF2	1
Jenapharm /Gehe	Neribas® fat ointment	YY0282F	1
Jenapharm/	Neribas® fat ointment	YY011K0	1
Jenapharm/AHCA	Neribas® fat ointment	YY0282F	2
Jenapharm/AHCA	Neribas® fat ointment	YY02L7L	2
Jenapharm/Ahd	Neribas® fat ointment	YYo11Ko	1
Jenapharm/Anzag	Neribas® fat ointment	YY0282F	1
Jenapharm/Phönix	Neribas® fat ointment	YYOOK7C	1
Jenapharm/Phönix	Neribas® fat ointment	YY0282F	1
Leo Pharma	Neribas® fat ointment	YY0431T	1
Noweda	Neribas® fat ointment	YY0282F	4
Phoenix	Neribas® fat ointment	YY00K7C	1
Phoenix WE 24.04.17 -7,…	Neribas® fat ointment	YY019KR	1
PhönixWE:18.01.2017 E…	Neribas® fat ointment	YY016LP	1
Römerapo.	Neribas® fat ointment	YY01TF2	1
Caelo	Protegin® XN	3091208	1
Caelo	Protegin® XN	11022403	1
Caelo	Protegin® XN	12229201	5
Caelo	Protegin® XN	11196802	1
Caelo	Protegin® XN	8031305	1
Caelo	Protegin® XN	12229211	5
Caelo	Protegin® XN	25061301	1
Caelo	Protegin® XN	12229210	1

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Supplier	Substance	Batch	Spectra
Caelo	Protegin® XN	12229209	1
Caelo	Protegin® XN	13081902	3
Caelo	Protegin® XN	13081903	1
Caelo	Protegin® XN	13081908	1
Caelo	Protegin® XN	6012014A	1
Caelo	Protegin® XN	20011402	1
Caelo	Protegin® XN	13081904	2
Caelo	Protegin® XN	13091906	1
Caelo	Protegin® XN	13081907	3
Caelo	Protegin® XN	14220204	3
Caelo	Protegin® XN	26031509	1
Caelo	Protegin® XN	14341301	3
Caelo	Protegin® XN	14220208	4
Caelo	Protegin® XN	14220206	2
Caelo	Protegin® XN	15252703	5
Caelo	Protegin® XN	15252702	2
Caelo	Protegin® XN	16026703	3
Caelo	Protegin® XN	16026707	6
Caelo	Protegin® XN	16026706	1
Caelo	Protegin® XN	16164505	4
Caelo	Protegin® XN	16164503	2
Caelo	Protegin® XN	17256702	1
Caelo	Protegin® XN	18059501	10
Caelo	Protegin® XN	18059511	2
Caelo	Protegin® XN	19109002	11
Caelo	Protegin® XN	20001749001	2
Caelo	Protegin® XN	20001749003	1
Caelo	Protegin® XN	19109001	4
Caelo	Protegin® XN	11196805	1
Caelo	Protegin® XN	20001749005	1
Caelo	Protegin® XN	16026704	4
Caelo	Protegin® XN	18059512	3
Caelo	Protegin® XN	14220209	4
Caelo	Protegin® XN	16026702	5
Caelo	Protegin® XN	191092002	3
Caelo	Protegin® XN	13081906	6
Caelo	Protegin® XN	14220203	3
Caelo	Protegin® XN	16026709	2
Caelo	Protegin® XN	16164501	1
Caelo	Protegin® XN	16164504	1
Caelo	Protegin® XN	17258707	3
Caelo	Protegin® XN	18059502	10
Caelo	Protegin® XN	14341302	1
Caelo	Protegin® XN	11196801	1
Caelo	Protegin® XN	13344401	6
Caelo	Protegin® XN	16164506	2
Caelo	Protegin® XN	18059507	5
Caelo	Protegin® XN	17258705	1
Caelo	Protegin® XN	17258708	1
Fagron	Protegin® XN	18059501	1
Caelo	Protegin® XN	14220202	5
Caelo	Protegin® XN	16026701	6
Caelo	Protegin® XN	18059505	1
Caelo	Protegin® XN	1805907	1
Caelo	Protegin® XN	18059509	1
Caelo	Protegin® XN	19110201	6
Caelo	Protegin® XN	18059503	2
Caelo	Protegin® XN	19109003	2
Caelo	Protegin® XN	19110202	10
Caelo	Protegin® XN	11196702	2

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Supplier	Substance	Batch	Spectra
Caelo	Protegin® XN	13081905	11
Caelo	Protegin® XN	14220201	1
Caelo	Protegin® XN	1805901	1
Caesar & Loretz	Protegin® XN	19110201	1
Caesar & Loretz GmbH	Protegin® XN	18059511	1
Caesar & Loretz GmbH	Protegin® XN	18059512	3
Caesar & Loretz GmbH	Protegin® XN	19109001	1
Caesar & Loretz GmbH	Protegin® XN	18059501	1
Caesar & Loretz GmbH	Protegin® XN	18059507	1
Caesar & Loretz GmbH	Protegin® XN	19109002	2
Caesar & Loretz GmbH	Protegin® XN	19110202	7
Caesar & Loretz GmbH / ...	Protegin® XN	19110202	2
Caesar & Loretz GmbH / ...	Protegin® XN	19110201	1
Caesar & Loretz GmbH/ N...	Protegin® XN	18059507	1
Fagron	Protegin® XN	18059507	1
Gehe	Protegin® XN	12229201	1
Gehe	Protegin® XN	12229211	1
Gehe	Protegin® XN	16026701	2
GEHE	Protegin® XN	18059507	1
Hedinger/Phönix	Protegin® XN	18059501	1
Ichthyol-Gesellschaft	Protegin® XN	17258703	1
Kehr	Protegin® XN	1805607	1
Caelo	Protegin® XN	16164502	2
Klenk	Protegin® XN	18059502	1
krieger	Protegin® XN	19110202	1
Phoenix	Protegin® XN	19110202	1
Phönix	Protegin® XN	11196706	1
Phönix	Protegin® XN	13081901	3
Phönix	Protegin® XN	16026707	1
PHÖNIX	Protegin® XN	18059501	1
Phönix 12.03.2013	Protegin® XN	12229205	1
Phönix, 07.11.13	Protegin® XN	12229210	1
Caelo	Protegin® XN	14220205	6
Caelo	Marjoram ointment	12123001	7
Caelo	Marjoram ointment	14089901	8
Jenapharm	Neribas® fat ointment	YY01TF2	1
	Protegin® XN	2711E-03598	1
Caelo	Protegin® XN	13344402	11
Caelo	Protegin® XN	13081901	4
Caelo	Protegin® XN	17258703	3
Euro OTC	Protegin® XN		1

- 7935 spectra from 714 *Apo-Ident* customers from a total of 3347 batches from a further 145 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	880	0	23 625
Type B	0	760	0	20 001
Type C	0	649	16	7935

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.3182 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 99.2105 %)
Type C	100.0000 % (> 98.7849 %)	97.5940 % (> 97.1429 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
White paraffin oil	12.33	–
Wax ointment (stabilised)	28.37	–
Lygal® head ointment N 3%	31.22	–
Salicylic white paraffin 10%	59.08	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
35069	35069	0.00	22.44
35071	35071	0.00	23.17
32473	32473	0.00	31.10
33130	33130	0.00	30.80
34966	34966	0.00	34.70

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33131	33131	0.00	32.56
34783	34783	0.00	38.91
30881	30881	0.00	33.60
30926	30926	0.00	39.73
31443	31443	0.00	36.44
31112	31112	0.00	38.37
31475	31475	0.00	39.74
33921	33921	0.00	38.26
34963	34963	0.00	33.93
31013	31013	0.00	37.04
31858	31858	0.00	45.52
33986	33986	0.00	43.06
33634	33634	0.00	42.74
34967	34967	0.00	33.53
31489	31489	0.00	44.05
31872	31872	0.00	48.18

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 2.3-2021-01

Validated substance/substance group	**Fenistil® Gel**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31045-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Fenistil® Gel

Special notes

When selecting the *Fenistil® Gel* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fenistil® Gel	3	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Fenistil® Gel*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Euro OTC	Fenistil® Gel	U02364A	33638	40	not required
Novartis	Fenistil® Gel	N00927A	31045	40	not required
Novartis	Fenistil® Gel	R02021A	31767	60	not required

Validation samples

A total of 53 906 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 *Fenistil® Gel*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Fenistil® Gel*.
- 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	Fenistil® Gel	T02415A	32787	40
Euro OTC	Fenistil® Gel	T02416A	32825	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Fenistil® Gel*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Fenistil® Gel* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fenistil® Gel* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Fenistil® Gel* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Sebexol® cream lotion pH 5	16.06	–
Sebexol® basic pH 5 formula basis	21.40	–
SyrSpend® SF pH4 cherry aroma	22.33	–
Hans Karrer Hydrocream MicroSilver	23.34	–
Aloe vera gel, 10x concentrated	26.31	–
Bepanthen® solution	27.34	–
Retterspitz external	27.81	–
SyrSpend® SF pH4 aroma free	29.97	–
Water	31.99	–
Wofacutan wash lotion	34.08	–
Aloe Vera gel, 1:1	34.70	–
Excipial® U Hydrolotio	35.33	–
Dimeticone ointment 10% SR	37.04	–
Abitima® clinic face cream	50.34	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31045	31045	0.00	19.18
31767	31767	0.00	21.86
33638	33638	0.00	21.63

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 2.3-2021-01

Validated substance/substance group	**Fennel oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	`31140-2021-03-22`
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Fennel oil; Oleum foeniculum vulgare var. dulce

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Fennel oil	3	2	1

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Fennel oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Fennel oil	L16813D-111973BAG90451	31140	40	not required
Taoasis	Fennel oil	L35513DN-119762	31693	60	not required
Taoasis	Fennel oil	1806-125039	32795	40	not required

Validation samples

A total of 53 906 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 *Fennel oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Fennel oil*.
- 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
Taoasis	Fennel oil	1806-127213	32952	40
Taoasis	Fennel oil	1861-129086	33991	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Fennel oil*.

- 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
Taoasis	Fennel oil	2307-5296	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Fennel oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Fennel oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	74	6	20 721
Type C	0	1	0	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	92.5000 % (> 88.7500 %)
Type C	100.0000 % (> 98.8499 %)	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 *Fennel oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Anise oil, organic	15.76	–
Thuja oil	78.06	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31140	31140	0.00	85.11
31693	31693	0.00	84.73
32795	32795	0.00	20.14

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 2.3-2021-01

Validated substance/substance group	**Ginger oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	`30451-2021-03-22`
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ginger oil; Oleum zingiber officinalis

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ginger oil	4	1	1

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ginger oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Ginger oil	00552A27	34407	40	not required
Taoasis	Ginger oil	130114-110686BAG90451	30958	40	not required
Taoasis	Ginger oil	40592A-112718BAG90451	31142	40	not required
Taoasis	Ginger oil	1431020-124656	32270	40	not required

Validation samples

A total of 53 906 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 *Ginger oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 345 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ginger oil*.
- 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
Bombastus	Ginger oil	300690	32569	40
Bombastus	Ginger oil	300690	33014	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Ginger oil*.

- 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
Taoasis	Ginger oil	6454-92725	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ginger oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ginger oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	80	0	20 721
Type C	0	1	0	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8499 %)	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 *Ginger oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citus oil	17.80	–
Cedar wood oil	18.36	–
Hyssop oil	20.06	–
Vetiver bourbon oil	23.66	–
Marjoram oil	24.65	–
Angelica root oil	26.16	–
Myrtle oil	27.93	–
Lemon grass oil	30.64	–
Immortelle oil	32.79	–
Cypress oil	36.10	–
Carrot seed oil	37.15	–
Spearmint oil	38.18	–
Yarrow oil	40.31	–
Spruce needle oil	41.24	–
Cumin oil	44.90	–
Frankincense oil	45.85	–
Patchouli oil	47.09	–
Silver fir oil	47.37	–
Swiss pine oil	51.75	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
34407	34407	0.00	30.53
32270	32270	0.00	28.93
31142	31142	0.00	18.36
30958	30958	0.00	20.06

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 2.3-2021-01

Validated substance/substance group	**Grapefruit oil organic / Orange oil / Blood orange oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30960-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Grapefruit oil organic / Orange oil / Blood orange oil; Blood orange oil; Grapefruit oil, organic; Oleum citrus paradisi; Oleum citrus sinensis; Orange oil

Special notes

When selecting the *Grapefruit oil organic / Orange oil / Blood orange oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Blood orange oil	2	3	1
Grapefruit oil, organic	3	3	12
Orange oil	3	6	20

Second-stage model

For differentiation of the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Blood orange oil	00413G25	33761	40	not required
Taoasis	Blood orange oil	494J09	33759	40	not required
Apotheker Bau…	Grapefruit oil, …	7.99615.16.02	31853	60	not required
Taoasis	Grapefruit oil, …	31564-119383	31634	120	not required
Taoasis	Grapefruit oil, …	38755-122181	31781	60	not required
Primavera	Orange oil	00112K25	33805	40	not required
Taoasis	Orange oil	121109-110685BAG90451	30960	40	not required
Taoasis	Orange oil	33732-12088	31679	60	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 460 spectra of 8 reference samples from the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 8 different batches.
- 24 045 spectra from a total of 496 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 12 reference samples from the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil*.
- 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
Primavera	Blood orange oil	00318C26	34175	40
Primavera	Blood orange oil	00111H26	34296	31
Primavera	Blood orange oil	00013A27	34376	40
Apotheker Bauer & Cie	Grapefruit oil, organic	7.68413.17.012018-03	33019	40
Primavera	Grapefruit oil, organic	00553M26	34385	40
Taoasis	Grapefruit oil, organic	44040A-124468	32979	40
Primavera	Orange oil	00149A29	33956	40
Primavera	Orange oil	00058G26	34180	40
Primavera	Orange oil	00729L26	34392	40
Taoasis	Orange oil	43829C-124974	32790	40
Taoasis	Orange oil	44583A-126780	32902	40
Taoasis	Orange oil	011855A-1538	34105	40

- 20 330 spectra from a total of 435 batches from further 201 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 33 batches from the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil*.
- 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
Taoasis	Blood orange oil	1AR18M-3519	1
Taoasis	Grapefruit oil, organic	44040A-124468	1
Taoasis	Grapefruit oil, organic	40038-123110	1
Taoasis	Grapefruit oil, organic	44040A-127409	1
Taoasis	Grapefruit oil, organic	31564-120540	1
Taoasis	Grapefruit oil, organic	46701-128853	1
Taoasis	Grapefruit oil, organic	44040A-124467	1
Taoasis	Grapefruit oil, organic	47037-1144	2
Taoasis	Grapefruit oil, organic	47037-958	1
Taoasis	Grapefruit oil, organic	47037-1602	1
Taoasis	Grapefruit oil, organic	48566-1955	1
Taoasis	Grapefruit oil, organic	AR18-12022-6352	1
Taoasis/Taoasis	Grapefruit oil, organic	40238-123217	1
BerglandSanacorp	Orange oil	K602772	1
Bombastus	Orange oil	302428	1
Bombastus	Orange oil	298756	1
Taoasis	Orange oil	140129-116983	1
Taoasis	Orange oil	140129-118141	1
Taoasis	Orange oil	140129-118790	1
Taoasis	Orange oil	140129-118420	1
Taoasis	Orange oil	42861A-122532	1
Taoasis	Orange oil	122650-123643	1
Taoasis	Orange oil	42861A-121691	1
Taoasis	Orange oil	44583A-128241	1
Taoasis	Orange oil	43829C-124155	1
Taoasis	Orange oil	43829C-125351	1

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Supplier	Substance	Batch	Spectra
Taoasis	Orange oil	6193	1
Taoasis	Orange oil	45441A-1035	1
Taoasis	Orange oil	45451A-128935	1
Taoasis	Orange oil	45451A-1178	1
Taoasis	Orange oil	11855A-3824	1
Taoasis/Gehe	Orange oil	497J09	1
Taoasis/Taoasis	Orange oil	44583A-127488	1

- 8566 spectra from 735 *Apo-Ident* customers from a total of 3513 batches from a further 147 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Grapefruit oil organic / Orange oil / Blood orange oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 045
Type B	0	471	0	20 330
Type C	0	34	0	8566

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9600 %)	100.0000 % (> 98.6957 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 98.7261 %)
Type C	100.0000 % (> 98.7867 %)	100.0000 % (> 82.3529 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Grapefruit oil organic / Orange oil / Blood orange oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citric oil	16.89	–
Mandarin oil, green	43.92	–
Lime oil	58.11	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30960	30960	0.00	43.31
31679	31679	0.00	45.30
33805	33805	0.00	44.21
31634	31634	0.00	41.51
31781	31781	0.00	46.06
31853	31853	0.00	36.23
33759	33759	0.00	43.76
33761	33761	0.00	43.14

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 2.3-2021-01

Validated substance/substance group	**Hydrophilic ointments**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30634-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Hydrophilic ointments; Abitima® clinic body cream; Abitima® clinic face cream; Allergika® Base cream; Asche Basis® cream; Asche Basis® lotion; Base cream Taoasis; Dermatest base ointment; Dermatop® base cream; DMS® base cream classic; DMS® base cream high classic; DMS® base cream high classic plus; Eucerinum O/W basis; Eucerinum W/O basis; Excipial® hydro cream; Excipial® lipo cream; Excipial® U Lipolotio; Excipial® U10 Lipolotio; Fabitop® base cream; Hans Karrer Lipocream MicroSilver; Hans Karrer Lipolotion MicroSilver; Linola® body milk; Lipoderm® lotion; Neribas® cream; Neuroderm® care lotion; Neuroderm® moisturising cream

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Abitima® clinic body cream	4	3	31
Abitima® clinic face cream	3	1	23
Allergika® Base cream	2	1	5
Asche Basis® cream	3	2	240
Asche Basis® lotion	3	1	52
Base cream Taoasis	3	1	16
Dermatest base ointment	4	4	10
Dermatop® base cream	2	2	23
DMS® base cream classic	4	1	9
DMS® base cream high classic	3	2	14
DMS® base cream high classic plus	2	1	2
Eucerinum O/W basis	2	0	14
Eucerinum W/O basis	3	1	27
Excipial® hydro cream	3	1	85
Excipial® lipo cream	5	0	61
Excipial® U Lipolotio	4	2	181
Excipial® U10 Lipolotio	3	2	17
Fabitop® base cream	3	2	12
Hans Karrer Lipocream MicroSilver	3	2	1
Hans Karrer Lipolotion MicroSilver	3	2	5
Linola® body milk	3	2	0
Lipoderm® lotion	3	2	17
Neribas® cream	1	2	42
Neuroderm® care lotion	3	2	0
Neuroderm® moisturising cream	3	1	44

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Hydrophilic ointments*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Actavis	Abitima® clinic ...	110712	31058	40	not required
Actavis	Abitima® clinic ...	051112	31061	40	not required
Actavis	Abitima® clinic ...	070915	32997	40	not required
Actavis	Abitima® clinic ...	331017	33969	40	not required
Actavis	Abitima® clinic ...	46820	30845	40	not required
Actavis	Abitima® clinic ...	161464	33793	40	not required
Actavis	Abitima® clinic ...	170180	34360	40	not required
Allergika	Allergika® Base ...	11/082022	33668	40	not required
Allergika	Allergika® Base ...	10/082022	33669	40	not required
Chiesi	Asche Basis® cream	03117A	30713	40	not required
Chiesi	Asche Basis® cream	22197A	30775	40	not required
Chiesi	Asche Basis® cream	24220A	31085	40	not required
Chiesi	Asche Basis® lot...	21042A	30828	40	not required
Chiesi	Asche Basis® lot...	24049A	31068	40	not required
Chiesi	Asche Basis® lot...	64082A	33737	40	not required
Taoasis	Base cream Taoasis	121205-2276	31041	100	not required
Taoasis	Base cream Taoasis	130124-3021	31115	40	not required
Taoasis	Base cream Taoasis	141222-4350	31578	60	not required

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Supplier	Substance	Batch	Sample ID	Spectra	Certificate
P&M Cosmetics	Dermatest base o…	251115	31627	60	not required
P&M Cosmetics	Dermatest base o…	180317	31950	60	not required
P&M Cosmetics	Dermatest base o…	121217	33039	40	not required
P&M Cosmetics	Dermatest base o…	040622	35149	40	not required
Sanofi aventis	Dermatop® base c…	3F031A	31234	40	not required
Sanofi aventis	Dermatop® base c…	5F056A	32177	40	not required
Koko	DMS® base cream …	L026G13	31307	40	not required
Koko	DMS® base cream …	L034H15	31869	60	not required
Koko	DMS® base cream …	L003H16	32916	40	not required
Koko	DMS® base cream …	L009K17	33968	40	not required
Koko	DMS® base cream …	L010K13	31236	70	not required
Koko	DMS® base cream …	L032A14	31308	40	not required
Koko	DMS® base cream …	L041K15	31870	60	not required
Koko	DMS® base cream …	L014L13	31309	40	not required
Koko	DMS® base cream …	L003L15	32178	40	not required
Beiersdorf	Eucerinum O/W ba…	41830108WA	31539	60	not required
Beiersdorf	Eucerinum O/W ba…	64030208WA	33213	40	not required
Beiersdorf	Eucerinum W/O ba…	31230108WA	30993	40	not required
Beiersdorf	Eucerinum W/O ba…	53430208WA	32767	40	not required
Beiersdorf	Eucerinum W/O ba…	83730208WA	34359	40	not required
Spirig Pharma	Excipial® hydro …	I013	30725	40	not required
Spirig Pharma	Excipial® hydro …	N013	31089	40	not required
Spirig Pharma	Excipial® hydro …	T052	33208	40	not required
Galderma Labo…	Excipial® lipo c…	V051	33636	40	not required
Spirig Pharma	Excipial® lipo c…	I011	30726	40	not required
Spirig Pharma	Excipial® lipo c…	N017	31088	40	not required
Spirig Pharma	Excipial® lipo c…	R011	31520	60	not required
Spirig Pharma	Excipial® lipo c…	T081	33207	40	not required
Galderma Labo…	Excipial® U Lipo…	T122	33270	40	not required
Spirig Pharma	Excipial® U Lipo…	M042	30732	60	not required
Spirig Pharma	Excipial® U Lipo…	N031	31067	40	not required
Spirig Pharma	Excipial® U Lipo…	N085	31280	40	not required
Spirig Pharma	Excipial® U10 Li…	M021	30733	60	not required
Spirig Pharma	Excipial® U10 Li…	N025	31066	40	not required
Spirig Pharma	Excipial® U10 Li…	N047	31281	40	not required
Fontapharm	Fabitop® base cr…	6RWW2	31082	40	not required
Fontapharm	Fabitop® base cr…	GWWL3	31576	60	not required
Fontapharm	Fabitop® base cr…	GLWD5	33221	40	not required
Hans Karrer G…	Hans Karrer Lipo…	15003	33194	40	not required
Hans Karrer G…	Hans Karrer Lipo…	15005	33195	40	not required
Hans Karrer G…	Hans Karrer Lipo…	18002	34117	40	not required
Hans Karrer G…	Hans Karrer Lipo…	15003	31730	60	not required
Hans Karrer G…	Hans Karrer Lipo…	15008	31873	60	not required
Hans Karrer G…	Hans Karrer Lipo…	18005	34119	40	not required
Dr. Wolff	Linola® body milk	433240	31511	60	not required
Dr. Wolff	Linola® body milk	511750	31874	60	not required
Dr. Wolff	Linola® body milk	707930	34043	40	not required
Spirig Pharma	Lipoderm® lotion	K057	30635	40	not required
Spirig Pharma	Lipoderm® lotion	M065	31072	40	not required
Spirig Pharma	Lipoderm® lotion	R023	31535	60	not required
Intendis	Neribas® cream	21076A	30634	40	not required
Intendis	Neribas® cream	21076A	31050	40	not required
Intendis	Neribas® cream	21076A	31095	40	not required
Infectopharm	Neuroderm® care …	S041204.1	31070	40	not required
Infectopharm	Neuroderm® care …	S031505.1	31772	60	not required
Infectopharm	Neuroderm® care …	S071706.1	34044	40	not required
Infectopharm	Neuroderm® moist…	S041214.1	30722	40	not required
Infectopharm	Neuroderm® moist…	S021307.1	31102	40	not required
Infectopharm	Neuroderm® moist…	S101428.1	31761	60	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 3510 spectra of 77 reference samples from the substance/substance group *Hydrophilic ointments*. These samples are listed above in the *calibration samples* section. The reference samples come from 74 different batches.
- 20 995 spectra from a total of 432 batches from further 136 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 2220 spectra of 56 reference samples from the substance/substance group *Hydrophilic ointments*.
- Among them are spectra of independent samples from 38 batches from which no spectra 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
Actavis	Abitima® clinic body cream	072013	30736	40
Actavis	Abitima® clinic body cream	040116	32999	40
Actavis	Abitima® clinic body cream	150818	34363	40
Actavis	Abitima® clinic face cream	158584	32179	40
Allergika	Allergika® Base cream	09/072022	33670	40
Chiesi	Asche Basis® cream	63351A	32928	40
Chiesi	Asche Basis® cream	63354A	33435	40
Chiesi	Asche Basis® lotion	53075A	32715	40
Taoasis	Base cream Taoasis	161124-6322	32944	40
P&M Cosmetics	Dermatest base ointment	120911	30737	40
P&M Cosmetics	Dermatest base ointment	070615	31053	20
P&M Cosmetics	Dermatest base ointment	231115	31288	40
P&M Cosmetics	Dermatest base ointment	260820	34032	40
Sanofi aventis	Dermatop® base cream	5F057A	32717	40
Sanofi aventis	Dermatop® base cream	7F069A	33966	40
Koko	DMS® base cream classic	L003E16	32788	40
Koko	DMS® base cream high classic	L037K16	33433	40
Koko	DMS® base cream high classic...	L018D16	32827	40
Beiersdorf	Eucerinum W/O basis	72630108WA	33629	40
Spirig Pharma	Excipial® hydro cream	50235	33982	40

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Supplier	Substance	Batch	Sample ID	Spectra
Galderma Laboratorium G…	Excipial® U Lipolotio	V011	33298	40
Spirig Pharma	Excipial® U Lipolotio	T122	33204	40
Spirig Pharma	Excipial® U10 Lipolotio	T072	33205	40
Spirig Pharma	Excipial® U10 Lipolotio	50393	33980	40
Fontapharm	Fabitop® base cream	GRWW1	30835	40
Fontapharm	Fabitop® base cream	GLWD4	33869	40
Hans Karrer GmbH	Hans Karrer Lipocream MicroS…	17001	33196	40
Hans Karrer GmbH	Hans Karrer Lipocream MicroS…	16002	33197	40
Hans Karrer GmbH	Hans Karrer Lipolotion Micro…	16005	32753	40
Hans Karrer GmbH	Hans Karrer Lipolotion Micro…	18004	34118	40
Dr. Wolff	Linola® body milk	606430	32765	40
Dr. Wolff	Linola® body milk	609202	33258	40
Spirig Pharma	Lipoderm® lotion	V012	33248	40
Spirig Pharma	Lipoderm® lotion	V042	33985	40
Jenapharm	Neribas® cream	YY01FX3	33289	40
Jenapharm	Neribas® cream	YY01X64	33951	40
Infectopharm	Neuroderm® care lotion	S111514.1	32740	40
Infectopharm	Neuroderm® care lotion	S081610.1	33286	40
Infectopharm	Neuroderm® moisturising cream	S051612.1	32905	40
Actavis	Abitima® clinic body cream	040116	33791	40
Actavis	Abitima® clinic face cream	158584	32723	40
Actavis	Abitima® clinic face cream	158584	32998	40
Chiesi	Asche Basis® lotion	53075A	32926	40
Taoasis	Base cream Taoasis	161124-6322	32945	40
Koko	DMS® base cream classic	L003E16	32826	40
Koko	DMS® base cream high classic	L003H16	32789	40
Koko	DMS® base cream high classic	L037K16	33434	40
Beiersdorf	Eucerinum O/W basis	64030208WA	33212	40
Beiersdorf	Eucerinum O/W basis	64030208WA	33850	40
Beiersdorf	Eucerinum W/O basis	72630108WA	33922	40
Spirig Pharma	Excipial® hydro cream	I013	30836	40
Spirig Pharma	Excipial® hydro cream	N013	31277	40
Galderma Laboratorium G…	Excipial® lipo cream	V051	33637	40
Spirig Pharma	Excipial® lipo cream	N017	31276	40
Galderma Laboratorium G…	Excipial® U Lipolotio	T122	33269	40
Infectopharm	Neuroderm® moisturising cream	S051612.1	32906	40

- 18 581 spectra from a total of 402 batches from further 179 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 2375 spectra from 323 *Apo-Ident* customers from 965 batches from the substance/substance group *Hydrophilic ointments*.

- Among them are spectra of independent samples from 864 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.	Abitima® clinic body cream	260515	2
Abitima	Abitima® clinic body cream	52015/051112	1

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Supplier	Substance	Batch	Spectra
actavis	Abitima® clinic body cream	20912	2
actavis	Abitima® clinic body cream	60513	2
actavis	Abitima® clinic body cream	140113	1
actavis	Abitima® clinic body cream	70513	1
actavis	Abitima® clinic body cream	110517	1
Actavis	Abitima® clinic body cream	20912	1
Actavis	Abitima® clinic body cream	31114	2
Actavis	Abitima® clinic body cream	10915	4
Actavis	Abitima® clinic body cream	31015	2
Actavis	Abitima® clinic body cream	32018	1
Actavis / Gehe	Abitima® clinic body cream	110712	1
Actavis Deutschland GmbH	Abitima® clinic body cream	350313	2
Actavis Deutschland GmbH	Abitima® clinic body cream	31015	1
Actavis Deutschland GmbH	Abitima® clinic body cream	121115	1
Actavis Group PTC	Abitima® clinic body cream	260515	1
Actavis/	Abitima® clinic body cream	21015	1
Actavis/ Gehe	Abitima® clinic body cream	60513	1
actavis/ebert	Abitima® clinic body cream	110712	1
actavis/Gehe	Abitima® clinic body cream	112015	1
actavis/Gehe	Abitima® clinic body cream	110712	2
actavis/Gehe	Abitima® clinic body cream	60513	1
Actavis/Gehe	Abitima® clinic body cream	51112	1
Actavis/Gehe	Abitima® clinic body cream	81013	1
Actavis/Noweda	Abitima® clinic body cream	21015	1
Actavis/Sanacorp	Abitima® clinic body cream	110712	1
APL swift Service/AHD	Abitima® clinic body cream	251118	1
APL swift Service/Sanac…	Abitima® clinic body cream	90118	1
APL Swift/ Phö	Abitima® clinic body cream	131118	1
Astellas Pharma	Abitima® clinic body cream	190213	1
Balkanpharma	Abitima® clinic body cream	90118	2
Caelo	Abitima® clinic body cream	40116	1
GEHE	Abitima® clinic body cream	100116	2
GEHE	Abitima® clinic body cream	331017	2
Noweda/Actavis	Abitima® clinic body cream	90118	2
Fagron	Abitima® clinic body cream	110517	2
Fagron	Abitima® clinic body cream	241118	1
Fagron	Abitima® clinic body cream	251118	2
Puren	Abitima® clinic body cream	251118	1
Puren Ph./Gehe	Abitima® clinic body cream	131118	1
Puren Pharma / Phönix	Abitima® clinic body cream	251118	2
Puren Pharma GmbH	Abitima® clinic body cream	131118	2
Puren Pharma GmbH	Abitima® clinic body cream	13118	1
PUREN Pharma GmbH &CoKG…	Abitima® clinic body cream	90118	1
Puren Pharma/Noweda	Abitima® clinic body cream	90118	1
Puren/Phoenix	Abitima® clinic body cream	130118	1
Puren/Phoenix	Abitima® clinic body cream	261118	1
Roche/AHD	Abitima® clinic body cream	142620	1
Sanacorp	Abitima® clinic body cream	210612	1
Sanacorp	Abitima® clinic body cream	70512	1
Sanacorp	Abitima® clinic body cream	51112	1
Sanacorp	Abitima® clinic body cream	140113	1
Sanacorp	Abitima® clinic body cream	12015/110/12	1
actavis	Abitima® clinic face cream	148496	2
actavis	Abitima® clinic face cream	148495	1
actavis	Abitima® clinic face cream	150202	1
actavis	Abitima® clinic face cream	150203	2
Actavis	Abitima® clinic face cream	160670	1
Actavis / Anzag	Abitima® clinic face cream	148024	1
Actavis / Anzag	Abitima® clinic face cream	148503	1
Actavis / Anzag	Abitima® clinic face cream	150237	1

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Supplier	Substance	Batch	Spectra
Actavis / Gehe	Abitima® clinic face cream	161904	3
Actavis / Noweda	Abitima® clinic face cream	142371	1
actavis group	Abitima® clinic face cream	161468	1
Actavis/Gehe	Abitima® clinic face cream	148495	1
Actavis/GEHE	Abitima® clinic face cream	148051	1
Actavis/Noweda	Abitima® clinic face cream	161423	1
actavis/Phönix	Abitima® clinic face cream	159274	2
actavis/Phönix	Abitima® clinic face cream	164225	1
Actavis/Phönix	Abitima® clinic face cream	164225	1
Caelo	Abitima® clinic face cream	146735	1
Caelo	Abitima® clinic face cream	149666	2
Caelo	Abitima® clinic face cream	161468	2
Caelo	Abitima® clinic face cream	170180	1
Fagron	Abitima® clinic face cream	150204	1
Noweda	Abitima® clinic face cream	146735	1
Persano/Gehe	Abitima® clinic face cream	57792	1
Phoenix/actavis	Abitima® clinic face cream	148460	1
Puren	Abitima® clinic face cream	169356	1
Puren / Gehe	Abitima® clinic face cream	174292	1
Puren Pharma	Abitima® clinic face cream	169357	1
Puren/AHCA	Abitima® clinic face cream	164225	1
allergika pharma gmbH /...	Allergika® Base cream	8/072024	1
Allergika Pharma/Sanacorp	Allergika® Base cream	2012023	1
Allergika/Phönix	Allergika® Base cream	4/032023	1
Henry Lamotte / 2	Allergika® Base cream	14/102023	1
Kehr 22.09.2020	Allergika® Base cream	2/2025	1
Aenova / Noweda	Asche Basis® cream	62343A	1
AHD/Chiesi	Asche Basis® cream	92436A	1
All.Heal./Chiesi	Asche Basis® cream	24218A	1
Alliance Healthcare	Asche Basis® cream	33240A	1
Alliance Healthcare	Asche Basis® cream	33237A	1
Anzag	Asche Basis® cream	23204A	1
Anzag/ Chiesi	Asche Basis® cream	42269A	1
Anzag/ Chiesi GmbH	Asche Basis® cream	42273A	1
Anzag/ Chiesi GmbH	Asche Basis® cream	42272A	1
Asche Chiesi/Alliance	Asche Basis® cream	71374A	1
Caelo	Asche Basis® cream	41265B	1
Caelo	Asche Basis® cream	52323a	1
Caelo	Asche Basis® cream	53331A	1
Caelo	Asche Basis® cream	61341A	2
Caelo	Asche Basis® cream	64359A	1
Caelo	Asche Basis® cream	71372A	1
Caelo	Asche Basis® cream	74398A	1
Caelo	Asche Basis® cream	83411A	3
Caelo	Asche Basis® cream	82409A	1
Caelo	Asche Basis® cream	61340A	1
Caelo	Asche Basis® cream	91426A	1
Caelo	Asche Basis® cream	52306A	3
Caelo	Asche Basis® cream	61337A	1
Caelo	Asche Basis® cream	31226A	1
Caelo	Asche Basis® cream	64364A	2
Caelo	Asche Basis® cream	20170829Ma4	1
Caelo	Asche Basis® cream	52322A	3
Caelo	Asche Basis® cream	53330A	1
Caelo	Asche Basis® cream	61335A	1
Caelo	Asche Basis® cream	73386A	2
Caelo	Asche Basis® cream	31227A	1
Caelo	Asche Basis® cream	64363A	1
Caelo	Asche Basis® cream	53329A	1
Caelo	Asche Basis® cream	61338A	1

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Supplier	Substance	Batch	Spectra
Caelo	Asche Basis® cream	71367A	1
Caelo	Asche Basis® cream	74391A	1
Caelo	Asche Basis® cream	81402A	3
Caelo	Asche Basis® cream	83413A	1
Caelo	Asche Basis® cream	72380A	2
Chiese	Asche Basis® cream	24221A	1
Chiese	Asche Basis® cream	41259A	1
Chiese	Asche Basis® cream	1449A	1
Chiese / Gehe	Asche Basis® cream	74392A	1
Chiese/Gehe	Asche Basis® cream	72385A	1
Chiese/Phönix	Asche Basis® cream	82408A	1
chiesi	Asche Basis® cream	71374A	1
chiesi	Asche Basis® cream	82407A	1
chiesi	Asche Basis® cream	83413A	1
chiesi	Asche Basis® cream	84422A	1
chiesi	Asche Basis® cream	84423A	1
chiesi	Asche Basis® cream	94448A	1
Chiesi	Asche Basis® cream	23204A	1
Chiesi	Asche Basis® cream	24214A	2
Chiesi	Asche Basis® cream	24219A	1
Chiesi	Asche Basis® cream	23206A	1
Chiesi	Asche Basis® cream	14178A	1
Chiesi	Asche Basis® cream	31227A	2
Chiesi	Asche Basis® cream	32236A	1
Chiesi	Asche Basis® cream	32235A	1
Chiesi	Asche Basis® cream	32233A	4
Chiesi	Asche Basis® cream	31232A	1
Chiesi	Asche Basis® cream	24217A	1
Chiesi	Asche Basis® cream	33237A	1
Chiesi	Asche Basis® cream	33240A	1
Chiesi	Asche Basis® cream	33243A	1
Chiesi	Asche Basis® cream	34249A	1
Chiesi	Asche Basis® cream	34251A	3
Chiesi	Asche Basis® cream	34250A	1
Chiesi	Asche Basis® cream	34248A	1
Chiesi	Asche Basis® cream	33239A	2
Chiesi	Asche Basis® cream	41258A	2
Chiesi	Asche Basis® cream	41261A	1
Chiesi	Asche Basis® cream	41260A	2
Chiesi	Asche Basis® cream	42270A	1
Chiesi	Asche Basis® cream	30102014A	1
Chiesi	Asche Basis® cream	42272A	1
Chiesi	Asche Basis® cream	42271A	2
Chiesi	Asche Basis® cream	43280A	1
Chiesi	Asche Basis® cream	42275A	1
Chiesi	Asche Basis® cream	43278A	1
Chiesi	Asche Basis® cream	43287A	1
Chiesi	Asche Basis® cream	43262A	1
Chiesi	Asche Basis® cream	43279A	1
Chiesi	Asche Basis® cream	44290A	1
Chiesi	Asche Basis® cream	51294A	1
Chiesi	Asche Basis® cream	51300A	4
Chiesi	Asche Basis® cream	51296A	2
Chiesi	Asche Basis® cream	51305A	2
Chiesi	Asche Basis® cream	52307A	2
Chiesi	Asche Basis® cream	52308A	3
Chiesi	Asche Basis® cream	52309A	1
Chiesi	Asche Basis® cream	52322A	1
Chiesi	Asche Basis® cream	53331A	2
Chiesi	Asche Basis® cream	53326A	1

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Supplier	Substance	Batch	Spectra
Chiesi	Asche Basis® cream	52310A	2
Chiesi	Asche Basis® cream	54332A	2
Chiesi	Asche Basis® cream	53330A	1
Chiesi	Asche Basis® cream	61338A	1
Chiesi	Asche Basis® cream	53329A	1
Chiesi	Asche Basis® cream	62343A	3
Chiesi	Asche Basis® cream	63347A	5
Chiesi	Asche Basis® cream	63354A	1
Chiesi	Asche Basis® cream	63350A	1
Chiesi	Asche Basis® cream	63355A	1
Chiesi	Asche Basis® cream	64357A	3
Chiesi	Asche Basis® cream	64360A	2
Chiesi	Asche Basis® cream	71367A	3
Chiesi	Asche Basis® cream	64362A-20170704Ma4	1
Chiesi	Asche Basis® cream	64359A	1
Chiesi	Asche Basis® cream	64364A	1
Chiesi	Asche Basis® cream	71374A	1
Chiesi	Asche Basis® cream	71370A	2
Chiesi	Asche Basis® cream	72380A	1
Chiesi	Asche Basis® cream	72378A	1
Chiesi	Asche Basis® cream	72383A	1
Chiesi	Asche Basis® cream	73387A	2
Chiesi	Asche Basis® cream	74390A	2
Chiesi	Asche Basis® cream	74393A	2
Chiesi	Asche Basis® cream	74392A	1
Chiesi	Asche Basis® cream	74398A	2
Chiesi	Asche Basis® cream	81400A	2
Chiesi	Asche Basis® cream	1(81404A)	1
Chiesi	Asche Basis® cream	81399A	2
Chiesi	Asche Basis® cream	81401A	5
Chiesi	Asche Basis® cream	81403A	1
Chiesi	Asche Basis® cream	81402A	1
Chiesi	Asche Basis® cream	83411A	1
Chiesi	Asche Basis® cream	83412A	1
Chiesi	Asche Basis® cream	84417A	1
Chiesi	Asche Basis® cream	84424A	2
Chiesi	Asche Basis® cream	83415A	1
Chiesi	Asche Basis® cream	84419A	1
Chiesi	Asche Basis® cream	91425A	1
Chiesi	Asche Basis® cream	83413A	1
Chiesi	Asche Basis® cream	91429A	1
Chiesi	Asche Basis® cream	91431A	1
Chiesi	Asche Basis® cream	92434A	1
Chiesi	Asche Basis® cream	92436A	1
Chiesi	Asche Basis® cream	92432A	1
Chiesi	Asche Basis® cream	94448AI	1
Chiesi	Asche Basis® cream	94448AII	1
Chiesi	Asche Basis® cream	92437A	1
Chiesi	Asche Basis® cream	4003A	1
Chiesi	Asche Basis® cream	2456A	1
CHiesi	Asche Basis® cream	41264A	1
chiesi-	Asche Basis® cream	71372A20171127Ma13	1
chiesi-	Asche Basis® cream	72376A-20180830Ma8	1
Chiesi / Alliance Healt…	Asche Basis® cream	82410A	1
Chiesi / Gehe	Asche Basis® cream	33244A	1
Chiesi / Gehe	Asche Basis® cream	34252A	1
Chiesi / Gehe	Asche Basis® cream	41265A	1
Chiesi / Gehe	Asche Basis® cream	43281A	1
Chiesi / Gehe	Asche Basis® cream	42273A	1
Chiesi / Gehe	Asche Basis® cream	51292A	1

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Supplier	Substance	Batch	Spectra
Chiesi / Gehe	Asche Basis® cream	52314A	1
chiesi / Noweda	Asche Basis® cream	23213A	1
chiesi / Noweda	Asche Basis® cream	31222A	1
chiesi / Noweda	Asche Basis® cream	31225A	1
chiesi / Noweda	Asche Basis® cream	34250A	1
Chiesi / Noweda	Asche Basis® cream	33238A	1
Chiesi / Noweda	Asche Basis® cream	33246A	1
Chiesi / Noweda	Asche Basis® cream	51300A	1
Chiesi / Noweda	Asche Basis® cream	54332A	1
Chiesi / Noweda	Asche Basis® cream	71374A	1
Chiesi / Noweda	Asche Basis® cream	72380A	1
Chiesi / Noweda	Asche Basis® cream	73386A	2
Chiesi / Noweda	Asche Basis® cream	74393A	2
Chiesi / Noweda	Asche Basis® cream	81399A	2
Chiesi / Noweda	Asche Basis® cream	84417A	1
Chiesi / Noweda	Asche Basis® cream	91426A	1
Chiesi / Noweda	Asche Basis® cream	92435A	1
Chiesi / Noweda	Asche Basis® cream	92442A	1
CHIESI / Noweda	Asche Basis® cream	51299A	3
Chiesi / Phoenix	Asche Basis® cream	51300A	1
Chiesi / Phoenix	Asche Basis® cream	52323A	2
Chiesi / Phoenix WE: 06...	Asche Basis® cream	53325A	1
chiesi /Jenne	Asche Basis® cream	31227a	1
chiesi gmbh	Asche Basis® cream	72380A	1
chiesi gmbh	Asche Basis® cream	82410A	1
Chiesi GmbH	Asche Basis® cream	24214A	1
Chiesi GmbH	Asche Basis® cream	52319A	1
Chiesi GmbH	Asche Basis® cream	61335A	1
Chiesi GmbH	Asche Basis® cream	64363A	1
Chiesi GmbH	Asche Basis® cream	64365A	1
Chiesi GmbH	Asche Basis® cream	72379A	1
Chiesi GmbH	Asche Basis® cream	74394A	1
Chiesi GmbH	Asche Basis® cream	72382A	1
Chiesi GmbH	Asche Basis® cream	81402A	1
Chiesi GmbH	Asche Basis® cream	82407A	1
Chiesi GmbH	Asche Basis® cream	84422A	1
Chiesi GmbH	Asche Basis® cream	91426A	1
Chiesi GmbH	Asche Basis® cream	84419A	1
Chiesi GmbH	Asche Basis® cream	92439A	1
Chiesi GmbH	Asche Basis® cream	92437A	1
Chiesi GmbH / Anzag	Asche Basis® cream	31222A	1
Chiesi GmbH / Anzag	Asche Basis® cream	22196A	1
Chiesi GmbH / Anzag	Asche Basis® cream	31230A	1
Chiesi GmbH / Anzag	Asche Basis® cream	31229A	1
Chiesi GmbH / Anzag	Asche Basis® cream	31231A	2
Chiesi GmbH / Anzag	Asche Basis® cream	33244A	1
Chiesi GmbH / Anzag	Asche Basis® cream	34249A	1
Chiesi GmbH / Anzag	Asche Basis® cream	41260A	1
Chiesi GmbH / Anzag	Asche Basis® cream	41261A	1
Chiesi GmbH / Anzag	Asche Basis® cream	42268A	2
Chiesi GmbH / Anzag	Asche Basis® cream	74394A	1
Chiesi GmbH / Sanacorp	Asche Basis® cream	34247A	1
Chiesi GmBH/ Alliance H...	Asche Basis® cream	83415A	1
Chiesi GmbH/ Noweda	Asche Basis® cream	74396A	1
Chiesi GmbH/ Noweda	Asche Basis® cream	84418A	1
Chiesi GmbH/ Noweda	Asche Basis® cream	91425A	1
Chiesi GmbH/ Noweda	Asche Basis® cream	84420A	1
Chiesi GmbH/AHD	Asche Basis® cream	1453A	1
Sino Phyto	Asche Basis® cream	74394A	1
Sino Phyto	Asche Basis® cream	92436A	2

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Supplier	Substance	Batch	Spectra
Chiesi Sanacorp	Asche Basis® cream	81404A	1
Chiesi/	Asche Basis® cream	41266A	1
Chiesi/ Noweda	Asche Basis® cream	64358A	3
Chiesi/ Fiebig	Asche Basis® cream	63356A	1
Chiesi/ Fiebig	Asche Basis® cream	64363A	2
Chiesi/ Fiebig	Asche Basis® cream	72376A	2
Chiesi/ Fiebig	Asche Basis® cream	74392A	1
Chiesi/ Gehe	Asche Basis® cream	52323A	1
Chiesi/ Gehe	Asche Basis® cream	82410A	1
Chiesi/ Gehe	Asche Basis® cream	83411A	1
Chiesi/ Gehe	Asche Basis® cream	73386A	1
Chiesi/ Gehe	Asche Basis® cream	84424A	1
Chiesi/ Gehe	Asche Basis® cream	92435A	1
Chiesi/ Gehe	Asche Basis® cream	92436A	1
Chiesi/ Gehe	Asche Basis® cream	1453A	1
Chiesi/ Now	Asche Basis® cream	33240A	1
Chiesi/ Now	Asche Basis® cream	41259A	1
Chiesi/ Now	Asche Basis® cream	42273A	1
Chiesi/ Now	Asche Basis® cream	43283A	2
Chiesi/ Now	Asche Basis® cream	43282A	1
Chiesi/ Noweda	Asche Basis® cream	51294a	1
Chiesi/ Noweda	Asche Basis® cream	52307A	1
Chiesi/ Noweda	Asche Basis® cream	170420AB/63353A	1
Chiesi/ Noweda	Asche Basis® cream	170601ABC/64357A	1
Chiesi/ Noweda	Asche Basis® cream	170628ABC/64362A	1
Chiesi/ Noweda	Asche Basis® cream	170706ABC/64361A	1
Chiesi/ Noweda	Asche Basis® cream	170816AB/64364A	1
Chiesi/ Noweda	Asche Basis® cream	170927AB/71370A	1
Chiesi/ Noweda	Asche Basis® cream	171025AB/71371A	1
Chiesi/ Noweda	Asche Basis® cream	71371A	1
Chiesi/ Noweda	Asche Basis® cream	171228ABC/72376A	1
Chiesi/ Noweda	Asche Basis® cream	171215ABC/72376A	1
Chiesi/ Noweda	Asche Basis® cream	180219AB/72379A	1
Chiesi/ Noweda	Asche Basis® cream	73389A	1
Chiesi/ phoenix	Asche Basis® cream	33239A	1
Chiesi/ Phönix	Asche Basis® cream	84421A	1
Chiesi/ Sanacorp	Asche Basis® cream	92434A	1
Chiesi/ Sanacorp	Asche Basis® cream	93443A	1
Chiesi//Phönix	Asche Basis® cream	63354A	1
Chiesi/4	Asche Basis® cream	83412A	1
Chiesi/AEP	Asche Basis® cream	72385A	1
Chiesi/AEP	Asche Basis® cream	71368A	1
Chiesi/AEP	Asche Basis® cream	73386A	2
Chiesi/AEP	Asche Basis® cream	73388A	4
Chiesi/AEP	Asche Basis® cream	74394A	1
Chiesi/AEP	Asche Basis® cream	82405A	2
Chiesi/AEP	Asche Basis® cream	84421A	1
Chiesi/AEP	Asche Basis® cream	91428A	2
Chiesi/AHCA	Asche Basis® cream	74396A	2
Chiesi/AHCA	Asche Basis® cream	82409A	2
Chiesi/AHD	Asche Basis® cream	31222A	1
Chiesi/AHD	Asche Basis® cream	31223A	1
Chiesi/AHD	Asche Basis® cream	31224A	1
Chiesi/AHD	Asche Basis® cream	31228A	2
Chiesi/AHD	Asche Basis® cream	32234A	1
Chiesi/AHD	Asche Basis® cream	32235A	1
Chiesi/AHD	Asche Basis® cream	33238A	1
Chiesi/AHD	Asche Basis® cream	33242A	1
Chiesi/AHD	Asche Basis® cream	34247A	1
Chiesi/AHD	Asche Basis® cream	81404A	1

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Supplier	Substance	Batch	Spectra
Chiesi/Alliance	Asche Basis® cream	61338A	1
Chiesi/Alliance Healthc…	Asche Basis® cream	44290A	4
Chiesi/Alliance Healthc…	Asche Basis® cream	52323A	4
Chiesi/Alliance Healthc…	Asche Basis® cream	53329A	1
Chiesi/Anzag	Asche Basis® cream	24221A	1
Chiesi/Anzag	Asche Basis® cream	43282A	1
Chiesi/Anzag	Asche Basis® cream	51295A	1
Chiesi/Anzag	Asche Basis® cream	53329A	1
Chiesi/Anzag	Asche Basis® cream	53327A	1
Chiesi/Ebert	Asche Basis® cream	31224A	1
Chiesi/Fiebig	Asche Basis® cream	733864A	1
Chiesi/Fiebig	Asche Basis® cream	74396A	1
Chiesi/Fiebig	Asche Basis® cream	81400A	2
Chiesi/Fiebig	Asche Basis® cream	81399A	1
Chiesi/Fiebig	Asche Basis® cream	92436A	1
Chiesi/Fiebig	Asche Basis® cream	92434A	1
chiesi/gehe	Asche Basis® cream	31228A	1
chiesi/gehe	Asche Basis® cream	32236A	1
chiesi/gehe	Asche Basis® cream	33246A	2
Chiesi/Gehe	Asche Basis® cream	24218A	1
Chiesi/Gehe	Asche Basis® cream	24221A	4
Chiesi/Gehe	Asche Basis® cream	31224A	1
Chiesi/Gehe	Asche Basis® cream	32233A	1
Chiesi/Gehe	Asche Basis® cream	34248A	1
Chiesi/Gehe	Asche Basis® cream	34253A	1
Chiesi/Gehe	Asche Basis® cream	41262A	1
Chiesi/Gehe	Asche Basis® cream	41260A	1
Chiesi/Gehe	Asche Basis® cream	42271A	1
Chiesi/Gehe	Asche Basis® cream	43278A	1
Chiesi/Gehe	Asche Basis® cream	51300A	1
Chiesi/Gehe	Asche Basis® cream	51301A	1
Chiesi/Gehe	Asche Basis® cream	52307A	1
Chiesi/Gehe	Asche Basis® cream	63350A	1
Chiesi/Gehe	Asche Basis® cream	71371A	1
Chiesi/Gehe	Asche Basis® cream	72379A	1
Chiesi/Gehe	Asche Basis® cream	72381A	2
Chiesi/Gehe	Asche Basis® cream	74390A	1
Chiesi/Gehe	Asche Basis® cream	73388A	1
Chiesi/Gehe	Asche Basis® cream	81400A	1
Chiesi/Gehe	Asche Basis® cream	81401A	1
Chiesi/Gehe	Asche Basis® cream	81402A	1
Chiesi/Gehe	Asche Basis® cream	82408A	2
Chiesi/Gehe	Asche Basis® cream	82409A	2
Chiesi/Gehe	Asche Basis® cream	83413A	2
Chiesi/Gehe	Asche Basis® cream	84420A	1
Chiesi/Gehe	Asche Basis® cream	941426A	1
Chiesi/Gehe	Asche Basis® cream	91426A	2
Chiesi/Gehe	Asche Basis® cream	91429A	2
Chiesi/Gehe	Asche Basis® cream	91430A	2
Chiesi/Gehe	Asche Basis® cream	91425A	1
Chiesi/Gehe	Asche Basis® cream	92434A	1
Chiesi/Gehe	Asche Basis® cream	92439A	1
Chiesi/Insel	Asche Basis® cream	74391A	1
Chiesi/Kehr	Asche Basis® cream	81402A	2
Chiesi/Kehr	Asche Basis® cream	82409A	1
Chiesi/Kehr	Asche Basis® cream	83416A	1
Chiesi/Kehr	Asche Basis® cream	83414A	1
Chiesi/Kehr	Asche Basis® cream	84421A	2
Chiesi/Kehr	Asche Basis® cream	84423A	1
Chiesi/Kehr	Asche Basis® cream	84422A	1

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Supplier	Substance	Batch	Spectra
Chiesi/Kehr	Asche Basis® cream	91427A	1
Chiesi/Kehr	Asche Basis® cream	92432A	2
Chiesi/Kehr	Asche Basis® cream	92439A	2
Chiesi/Kehr	Asche Basis® cream	2460A	2
Chiesi/Krieger	Asche Basis® cream	64363A	1
Chiesi/Krieger	Asche Basis® cream	72379A	1
Chiesi/Krieger	Asche Basis® cream	72383A	1
Chiesi/Krieger	Asche Basis® cream	72384A	1
Chiesi/Krieger	Asche Basis® cream	74396A	1
Chiesi/Krieger	Asche Basis® cream	81403A	1
Chiesi/Krieger	Asche Basis® cream	82407A	1
Chiesi/Krieger	Asche Basis® cream	82409A	1
Chiesi/Krieger	Asche Basis® cream	91427A	1
Chiesi/Krieger	Asche Basis® cream	92435A	1
Chiesi/Krieger	Asche Basis® cream	91430A	2
Chiesi/Krieger	Asche Basis® cream	91431A	1
Chiesi/Krieger	Asche Basis® cream	93444A	1
Chiesi/Krieger	Asche Basis® cream	1452A	2
Chiesi/Krieger	Asche Basis® cream	1449A	1
Chiesi/Noweda	Asche Basis® cream	31224A	1
Chiesi/Noweda	Asche Basis® cream	31229A	1
Chiesi/Noweda	Asche Basis® cream	31232A	1
Chiesi/Noweda	Asche Basis® cream	33237A	1
Chiesi/Noweda	Asche Basis® cream	34247A	1
Chiesi/Noweda	Asche Basis® cream	41258A	1
Chiesi/Noweda	Asche Basis® cream	42275A	1
Chiesi/Noweda	Asche Basis® cream	43280A	1
Chiesi/Noweda	Asche Basis® cream	44288A	1
Chiesi/Noweda	Asche Basis® cream	52306A	2
Chiesi/Noweda	Asche Basis® cream	52318A	1
Chiesi/Noweda	Asche Basis® cream	53329A	1
Chiesi/Noweda	Asche Basis® cream	52318a	1
Chiesi/Noweda	Asche Basis® cream	6234A	1
Chiesi/Noweda	Asche Basis® cream	63347A	1
Chiesi/Noweda	Asche Basis® cream	170421AB/63353A	1
Chiesi/Noweda	Asche Basis® cream	171211AB/72376A	1
Chiesi/Noweda	Asche Basis® cream	180112ABC/72378A	1
Chiesi/Noweda	Asche Basis® cream	180322AB/72382A	1
Chiesi/Noweda	Asche Basis® cream	74394A	1
Chiesi/Noweda	Asche Basis® cream	84424A	2
Chiesi/Phoenix	Asche Basis® cream	24215A	1
Chiesi/Phoenix	Asche Basis® cream	31225A	1
Chiesi/Phoenix	Asche Basis® cream	31227A	2
Chiesi/Phoenix	Asche Basis® cream	31229A	1
Chiesi/Phoenix	Asche Basis® cream	32233A	1
Chiesi/Phoenix	Asche Basis® cream	43278A	1
Chiesi/Phoenix	Asche Basis® cream	71368A	1
Chiesi/Phoenix	Asche Basis® cream	72377A	1
Chiesi/Phoenix	Asche Basis® cream	72383A	1
Chiesi/Phoenix	Asche Basis® cream	74394A	1
Chiesi/Phönix	Asche Basis® cream	53329A	1
Chiesi/Phönix	Asche Basis® cream	61334A	1
Chiesi/Phönix	Asche Basis® cream	64358A	1
Chiesi/Phönix	Asche Basis® cream	71367A	1
Chiesi/Phönix	Asche Basis® cream	72375A	1
Chiesi/Phönix	Asche Basis® cream	72385A	2
Chiesi/Phönix	Asche Basis® cream	73388A	2
Chiesi/Phönix	Asche Basis® cream	74394A	1
Chiesi/Phönix	Asche Basis® cream	81404A	2
Chiesi/Phönix	Asche Basis® cream	81400A	1

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Supplier	Substance	Batch	Spectra
Chiesi/Phönix	Asche Basis® cream	82405A	1
Chiesi/Phönix	Asche Basis® cream	81402A	1
Chiesi/Phönix	Asche Basis® cream	81401A	2
Chiesi/Phönix	Asche Basis® cream	82407A	1
Chiesi/Phönix	Asche Basis® cream	84417A	1
Chiesi/Phönix	Asche Basis® cream	83412A	2
Chiesi/Phönix	Asche Basis® cream	83416A	3
Chiesi/Phönix	Asche Basis® cream	84418A	2
Chiesi/Phönix	Asche Basis® cream	84420A	2
Chiesi/Phönix	Asche Basis® cream	84421A	1
Chiesi/Phönix	Asche Basis® cream	84419A	3
Chiesi/Phönix	Asche Basis® cream	91426A	1
Chiesi/Phönix	Asche Basis® cream	92435A	1
Chiesi/Phönix	Asche Basis® cream	91427A	1
Chiesi/Phönix	Asche Basis® cream	91429A	1
Chiesi/Phönix	Asche Basis® cream	91425A	1
Chiesi/Phönix	Asche Basis® cream	92434A	1
Chiesi/Phönix	Asche Basis® cream	92432A	1
Chiesi/Phönix	Asche Basis® cream	92441A	1
Chiesi/Phönix	Asche Basis® cream	92437A	3
Chiesi/Phönix	Asche Basis® cream	93443A	1
Chiesi/Phönix	Asche Basis® cream	2459A	1
Chiesi/Phönix	Asche Basis® cream	1451A	1
Chiesi/Phönix WE:19.05....	Asche Basis® cream	64357A	1
Chiesi/Phönix WE:20.06....	Asche Basis® cream	64362A	2
Chiesi/Phönix WE:27.05....	Asche Basis® cream	52309A	1
Chiesi/Sanacorp	Asche Basis® cream	31227A	1
Chiesi/Sanacorp	Asche Basis® cream	74394A	1
Chiesi/Sanacorp	Asche Basis® cream	82408A	1
Chiesi/Sanacorp	Asche Basis® cream	83412A	1
Chiesi/Sanacorp	Asche Basis® cream	83413A	1
Chiesi/Sanacorp	Asche Basis® cream	84418A	1
Chiesi/Sanacorp 311.15	Asche Basis® cream	51305A	3
Chiesi/Sanacorp WE:06.0...	Asche Basis® cream	52317A	1
Spangropharm	Asche Basis® cream	82093A	1
Chiesi/V.d.L.	Asche Basis® cream	34250A	1
Chiesi/VDL	Asche Basis® cream	92436A	1
Chiesi/VDL	Asche Basis® cream	1455A	1
Chiesie	Asche Basis® cream	84417A	1
Chiesie	Asche Basis® cream	92436A	1
Chiesie	Asche Basis® cream	92439A	1
Chiesi-Fa.Gehe	Asche Basis® cream	71372A	1
Chiesi-Fa.Gehe	Asche Basis® cream	81401A-A20190115Ma11	1
Chiesi-Fa.Gehe 19.6.18	Asche Basis® cream	74391A-20180830Ma7	1
Chisei	Asche Basis® cream	72382A	1
Chisesi	Asche Basis® cream	52310A	1
Chisesi/Noweda	Asche Basis® cream	53331A	1
Chisesi/Noweda	Asche Basis® cream	61338A	1
Chisesi/Noweda	Asche Basis® cream	71367A	1
Chisi	Asche Basis® cream	23203A	1
Chisie/ Jenne	Asche Basis® cream	91431A	1
Chisie/VDL	Asche Basis® cream	84417A	2
Euro OTC	Asche Basis® cream	3229A	1
Euro OTC	Asche Basis® cream	61337A	2
Fa.Gehe	Asche Basis® cream	20160727Ma4	1
Fagron	Asche Basis® cream	63353A	1
Fiebig	Asche Basis® cream	83413A	3
Fiebig	Asche Basis® cream	84421A	1
Fiebig	Asche Basis® cream	84420A	1
Fiebig	Asche Basis® cream	91428A	2

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Supplier	Substance	Batch	Spectra
Fiebig/Chiesi GmbH	Asche Basis® cream	73388A	1
Fiebig/Chiesi GmbH	Asche Basis® cream	81404A	1
Galaderma/Krieger	Asche Basis® cream	17370A	1
Gehe	Asche Basis® cream	32236A	1
Gehe	Asche Basis® cream	33244A	1
Gehe	Asche Basis® cream	52321A	1
Gehe	Asche Basis® cream	61334A	1
Gehe	Asche Basis® cream	64358A	2
Gehe	Asche Basis® cream	64360A	1
GEHE	Asche Basis® cream	73387A	2
GEHE	Asche Basis® cream	81399A	1
GEHE	Asche Basis® cream	82410A	1
Gehe/Chesie	Asche Basis® cream	52318A	2
Gehe/Chiesi	Asche Basis® cream	32233A	1
Gehe/Chiesi	Asche Basis® cream	51296A	1
Gehe/Chiesi	Asche Basis® cream	84418A	2
Gehe/Chiesi	Asche Basis® cream	1452A	1
Gehe/Chiesi	Asche Basis® cream	92440A	1
Gehe-Chiesi	Asche Basis® cream	52308A	1
Gepepharm/VDL	Asche Basis® cream	81399A	1
Hedinger	Asche Basis® cream	74398A	1
Hedinger/Noweda	Asche Basis® cream	82405A	1
Ichthyol/Sanacorp	Asche Basis® cream	24221A	1
Insel	Asche Basis® cream	72378A	1
krieger	Asche Basis® cream	92436A	1
Lamotte / Gehe	Asche Basis® cream	34247A	1
Noweda	Asche Basis® cream	81399A	1
Noweda	Asche Basis® cream	82410A	1
Noweda	Asche Basis® cream	83411A	2
Noweda	Asche Basis® cream	84417A	4
Noweda	Asche Basis® cream	84424A	3
Noweda	Asche Basis® cream	92435A	2
Noweda	Asche Basis® cream	92436A	4
Noweda	Asche Basis® cream	92442A	2
Noweda	Asche Basis® cream	1453A	2
Noweda	Asche Basis® cream	1455A	2
Noweda	Asche Basis® cream	3461A	2
Noweda/Apomix	Asche Basis® cream	92433A	1
noweda/chiesi	Asche Basis® cream	52306A	1
Noweda/Chiesi	Asche Basis® cream	73386A	1
Noweda/Chiesi	Asche Basis® cream	82410A	1
Noweda/Chiesi	Asche Basis® cream	84424A	1
Noweda/Chiesi	Asche Basis® cream	94448A	1
Phoenix	Asche Basis® cream	53331A	1
Phoenix	Asche Basis® cream	54332A	1
Phoenix WE 13.04.17 -7,...	Asche Basis® cream	63353A	2
Phoenix WE: 08.11.17 10...	Asche Basis® cream	71372A	1
Phoenix WE: 09.10.17 50...	Asche Basis® cream	71368A	1
Phoenix/Chiesi	Asche Basis® cream	33246A	1
Phoenix/Chiesi	Asche Basis® cream	61333A	1
Phoenix/Chiesi	Asche Basis® cream	64358A	1
Phoenix/Chiesi	Asche Basis® cream	73387A	1
Phoenix/Chiesi	Asche Basis® cream	81399A	1
Phönix	Asche Basis® cream	322344	1
Phönix	Asche Basis® cream	81404A	1
PHÖNIX	Asche Basis® cream	62343A	1
PHÖNIX	Asche Basis® cream	73386A	1
Phönix /Chiesi	Asche Basis® cream	81402A	1
phönix WE: 28.08.17 EK...	Asche Basis® cream	64365A	2
PhönixWE:3.02.2017 EK...	Asche Basis® cream	63350A	1

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Supplier	Substance	Batch	Spectra
Sanacoro W.E:01.03.18 ...	Asche Basis® cream	72378A	1
Sanacoro W.E:01.03.18 ...	Asche Basis® cream	72379A	2
Sanacorp	Asche Basis® cream	53327A	1
SANACORP	Asche Basis® cream	84417A	2
SANACORP	Asche Basis® cream	92435A	1
Sanacorp /100ml	Asche Basis® cream	72382A	2
Sanacorp EK:8,07 EUR...	Asche Basis® cream	64363A	1
Sanacorp EK:8,07 EUR...	Asche Basis® cream	64364A	1
Sanacorp / Wolff	Asche Basis® cream	82A05A	1
Sanacorp /Chiesi	Asche Basis® cream	84418A	1
Sanacorp W.E: 02.02.18 ...	Asche Basis® cream	72377A	1
Sanacorp WE 20.02.17 -7...	Asche Basis® cream	63351A	3
WE Sanacorp	Asche Basis® cream	61341A	1
WE: Phoenix 07.10.2016 ...	Asche Basis® cream	61340A	1
WE: Phoenix 23.09.2016 ...	Asche Basis® cream	61339A	1
WE:Phönix28.07.2016 E...	Asche Basis® cream	61336A	1
Wolff/ Sanacorp	Asche Basis® cream	810201	1
Wolff/Gehe	Asche Basis® cream	71366A	1
Wolff/Gehe	Asche Basis® cream	64365A-20171106Ma10	1
Aenov Groupe	Asche Basis® lotion	40000200790	1
Aenova	Asche Basis® lotion	93102A	1
Alliance Healthcare	Asche Basis® lotion	63981A	1
Alliance Healthcare	Asche Basis® lotion	73087A	1
Alliance Healthcare	Asche Basis® lotion	73089A	1
Alliance Healthcare	Asche Basis® lotion	82094A	2
Alliance Healthcare	Asche Basis® lotion	91098A	3
Alliance Healthcare	Asche Basis® lotion	91099A	1
Alliance Healthcare	Asche Basis® lotion	92100A	3
Alliance Healthcare	Asche Basis® lotion	93103A	4
Asche Chiesi/Alliance	Asche Basis® lotion	73087A	1
Caelo	Asche Basis® lotion	41059A	2
Caelo	Asche Basis® lotion	33055A	3
Caelo	Asche Basis® lotion	32054A	1
Caelo	Asche Basis® lotion	53075A	1
Caelo	Asche Basis® lotion	53072A	1
Caelo	Asche Basis® lotion	53073A	1
Caelo	Asche Basis® lotion	73089A	1
Chiese	Asche Basis® lotion	41060A	1
chiesi	Asche Basis® lotion	84095A	1
Chiesi	Asche Basis® lotion	333056A	2
Chiesi	Asche Basis® lotion	32054A	2
Chiesi	Asche Basis® lotion	41059A	1
Chiesi	Asche Basis® lotion	43066A	1
Chiesi	Asche Basis® lotion	53072A	1
Chiesi	Asche Basis® lotion	53075A	2
Chiesi	Asche Basis® lotion	53073A	1
Chiesi	Asche Basis® lotion	61077A	1
Chiesi	Asche Basis® lotion	46082A	1
Chiesi	Asche Basis® lotion	730874	1
Chiesi	Asche Basis® lotion	73088A	3
Chiesi	Asche Basis® lotion	75085A	1
Chiesi	Asche Basis® lotion	73088a	1
Chiesi	Asche Basis® lotion	82094A	1
Chiesi	Asche Basis® lotion	92101A	1
Chiesi GmbH	Asche Basis® lotion	53071A	3
Chiesi GmbH	Asche Basis® lotion	53072A	2
Chiesi GmbH	Asche Basis® lotion	53074A	1
Chiesi GmbH	Asche Basis® lotion	61076A	2
Chiesi GmbH	Asche Basis® lotion	63078A	2
Chiesi GmbH	Asche Basis® lotion	63079A	2

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Supplier	Substance	Batch	Spectra
Chiesi GmbH	Asche Basis® lotion	63980A	1
Chiesi GmbH	Asche Basis® lotion	73087A	1
Chiesi GmbH	Asche Basis® lotion	92100A	1
Chiesi GmbH / Phönix	Asche Basis® lotion	51067A	1
Chiesi GmbH/Gehe	Asche Basis® lotion	53072A	1
Chiesi/ Noweda	Asche Basis® lotion	64082A	1
Chiesi/ Fiebig	Asche Basis® lotion	63980A	1
Chiesi/ Phönix	Asche Basis® lotion	43066A	1
Chiesi/AHD	Asche Basis® lotion	24049A	1
Chiesi/Alliance	Asche Basis® lotion	63981A	1
Chiesi/Anzag	Asche Basis® lotion	53075A	2
Chiesi/E+J	Asche Basis® lotion	64082A	1
Chiesi/Fa.Gehe	Asche Basis® lotion	53075A	1
Chiesi/Fiebig	Asche Basis® lotion	53073A	2
Chiesi/Fiebig	Asche Basis® lotion	53074A	1
Chiesi/Fiebig	Asche Basis® lotion	63980A	1
Chiesi/Fiebig	Asche Basis® lotion	73086A	1
Chiesi/Fiebig	Asche Basis® lotion	82092A	2
Chiesi/Fiebig	Asche Basis® lotion	92100A	1
chiesi/gehe	Asche Basis® lotion	33056A	2
chiesi/gehe	Asche Basis® lotion	34058A	1
Chiesi/Gehe	Asche Basis® lotion	23047A	1
Chiesi/Krieger	Asche Basis® lotion	64082A	1
Chiesi/Krieger	Asche Basis® lotion	82092A	1
Chiesi/Noweda	Asche Basis® lotion	61077A	1
Chiesi/Noweda	Asche Basis® lotion	64082A	1
Chiesi/Noweda	Asche Basis® lotion	71083A	1
Chiesi/Noweda	Asche Basis® lotion	73089A	1
Chiesi/Phoenix	Asche Basis® lotion	52070A	1
Chiesi/Phoenix	Asche Basis® lotion	53071A	1
Chiesi/Phoenix	Asche Basis® lotion	64082A	1
Chiesi/Phönix	Asche Basis® lotion	53071A	1
Chiesi/Phönix	Asche Basis® lotion	53073A	1
Chiesi/Phönix	Asche Basis® lotion	63078A	1
Chiesi/Phönix	Asche Basis® lotion	63981A	1
Chiesi/Phönix	Asche Basis® lotion	73086A	2
Chiesi/Phönix	Asche Basis® lotion	84095A	2
Chiesi/Phönix	Asche Basis® lotion	82092A	1
Chiesi/Phönix	Asche Basis® lotion	92100A	1
Chiesi/Sanacorp	Asche Basis® lotion	91097A	1
Chiesie/Anzag	Asche Basis® lotion	32054A	1
Chiesi-Fa.Gehe	Asche Basis® lotion	64082A-20180112Ma3	1
Chiesi-Fa.Gehe	Asche Basis® lotion	73087A-20180206Ma9	1
Chiesi-Fa.Gehe	Asche Basis® lotion	73086A-20180206Ma8	1
Chiesi-Fa.Gehe	Asche Basis® lotion	82093A-A20181115Ma1	1
Chiesi-Fa.Gehe 19.7.18	Asche Basis® lotion	74090A-20180830Ma10	1
Ebert & Jacobi	Asche Basis® lotion	73088A	1
Fa.Gehe	Asche Basis® lotion	20160727Ma5	1
Fiebig	Asche Basis® lotion	91097A	1
Caelo	Asche Basis® lotion	63078A	1
Fiebig/Chiesi	Asche Basis® lotion	71083A	1
Fiebig/Chiesi	Asche Basis® lotion	71084A	3
Fiebig/Chiesi	Asche Basis® lotion	73087A	2
Fiebig/Chiesi	Asche Basis® lotion	84095A	1
Gehe	Asche Basis® lotion	82082A	1
Gehe Chiesi	Asche Basis® lotion	53075A-20160615Ma5	1
Caelo	Asche Basis® lotion	64082A	3
gehe/Chiesi	Asche Basis® lotion	43066A	1
Gehe/Chiesi	Asche Basis® lotion	93103A	1
Gehe20.10.15	Asche Basis® lotion	52070A	1

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Supplier	Substance	Batch	Spectra
Noweda	Asche Basis® lotion	63980A	1
Bombastus	Asche Basis® lotion	74091A	1
Caelo	Asche Basis® lotion	64082a	1
Phoenix	Asche Basis® lotion	52069A	1
PHÖNIX	Asche Basis® lotion	91098A	1
/Sanacorp	Base cream Taoasis	180718-7100	4
Bombastus	Base cream Taoasis	180307	1
Caelo	Base cream Taoasis	180924-8114	1
Caelo	Base cream Taoasis	171127-7290	1
Caelo	Base cream Taoasis	170110-6322	1
St. Martin/Taoasis	Base cream Taoasis	180924-8114	1
taoasis	Base cream Taoasis	180307-8030	1
Taoasis	Base cream Taoasis	150219-4350	1
Taoasis	Base cream Taoasis	150326-5079	1
Taoasis	Base cream Taoasis	161124-6322	1
Taoasis	Base cream Taoasis	170110-6322	1
Taoasis	Base cream Taoasis	160201-6027	1
Taoasis	Base cream Taoasis	170317-7031	1
Taoasis	Base cream Taoasis	170517-7100	1
Taoasis	Base cream Taoasis	171127-7290	1
Taoasis	Base cream Taoasis	181204-8333	1
Taoasis GmbH/ Taoasis	Base cream Taoasis	190916-9182	1
Taoasis/Phoenix	Base cream Taoasis	180718-7100	1
Taoasis/Sanacorp	Base cream Taoasis	170317-7031	3
Taoasis/Sanacorp	Base cream Taoasis	170517-7100	2
Taoasis/Sanacorp	Base cream Taoasis	1807187100	1
Taoasis/Sanacorp	Base cream Taoasis	171127-7290	10
Taoasis/Sanacorp	Base cream Taoasis	180924-8114	1
Taoasis/Sanacorp	Base cream Taoasis	180515-8030	1
Caelo	Dermatest base ointment	121217	1
Leyh GmbH	Dermatest base ointment	121217	1
P&M	Dermatest base ointment	241115	1
P&M Cosmetics	Dermatest base ointment	210915	1
P&M Cosmetics	Dermatest base ointment	260820	2
P&M Cosmetics/Alliance	Dermatest base ointment	160820	1
P&M Cosmetics/Alliance …	Dermatest base ointment	152241	1
P&M Cosmetics/Anzag	Dermatest base ointment	122631	1
p&m cosmetics/gehe	Dermatest base ointment	200419	1
P&M/Alliance	Dermatest base ointment	121217	1
P&M/Alliance	Dermatest base ointment	190317	1
P&M/Alliance	Dermatest base ointment	260820	2
Phoenix	Dermatest base ointment	260820	1
Sanacorp	Dermatest base ointment	70615	1
Sanacorp/Apomix	Dermatest base ointment	280821	1
Klindwort Apotheke Rath…	Dermatop® base cream	8F075A	1
Phönix	Dermatop® base cream	7F072A	2
Sanofi	Dermatop® base cream	4F046A	1
Sanofi	Dermatop® base cream	F092A	1
Sanofi / Gehe	Dermatop® base cream	4F046A	1
Sanofi Aventis	Dermatop® base cream	4F046A	1
Sanofi/AllianceHealthcare	Dermatop® base cream	F091A	2
Sanofi/Anzag	Dermatop® base cream	5F051A	1
Sanofi/Anzag	Dermatop® base cream	5F056A	1
Sanofi/Gehe	Dermatop® base cream	4F050A	1
Sanofi/Noweda	Dermatop® base cream	5F056A	1
Sanofi/Phönix	Dermatop® base cream	4F046A	1
Sanofi/Phönix	Dermatop® base cream	5F051A	1
Sanofi/Phönix	Dermatop® base cream	7F071A	1
Sanofi/Phönix	Dermatop® base cream	7F073A	2
Sanofi/Phönix	Dermatop® base cream	7F069A	1

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Supplier	Substance	Batch	Spectra
Sanofi/Phönix	Dermatop® base cream	8F074A	2
Sanofi/Phönix	Dermatop® base cream	8F079A	1
Sanofi/Phönix	Dermatop® base cream	8F078A	2
Sanofi/Phönix	Dermatop® base cream	8F081A	2
Sanofi/Phönix	Dermatop® base cream	8F076A	1
Sanofi/Phönix	Dermatop® base cream	8F084A	3
Sanofi/Phönix	Dermatop® base cream	8F083A	3
Sanofi/Phönix	Dermatop® base cream	8F082B	1
Sanofi/Phönix	Dermatop® base cream	9F086A	1
Sanofi/Phönix	Dermatop® base cream	8F082A	1
Sanofi/Phönix	Dermatop® base cream	9F087A	1
Sanofi/Phönix	Dermatop® base cream	9F089A	1
Sanofi/Sanacorp	Dermatop® base cream	7F071A	1
Sanofi-Aventis/Gehe	Dermatop® base cream	5F051A	1
Sanofi-Aventis/Phönix	Dermatop® base cream	6F065A	1
KOKO GmbH	DMS® base cream classic	L003E16	1
KOKO GmbH	DMS® base cream classic	L005A14	1
KOKO GmbH & Co KG	DMS® base cream classic	L062H18	6
KOKO GmbH & Co KG	DMS® base cream classic	L036I18	2
KOKO GmbH & Co KG	DMS® base cream classic	L036118	2
KOKO GmbH & Co KG	DMS® base cream classic	L036l18	1
koko GmbH EK: EUR 38,30 /...	DMS® base cream classic	L008F17	1
Koko GmBH&Co KG	DMS® base cream classic	L038J16	1
KoKo GmbH/KoKo Gmbh	DMS® base cream classic	11090E19	1
Caelo	DMS® base cream high classic	L010J15	1
Caelo	DMS® base cream high classic	L047117	4
KOKO	DMS® base cream high classic	L031A14	1
Koko Gmbh	DMS® base cream high classic	L019H17	1
Koko Gmbh	DMS® base cream high classic	L033J17	3
Koko Gmbh	DMS® base cream high classic	L031D18	1
Koko GmbH	DMS® base cream high classic	L031A14	1
KOKO Gmbh	DMS® base cream high classic	L010E17	10
KOKO Gmbh	DMS® base cream high classic	L019H17	5
KOKO Gmbh	DMS® base cream high classic	L008K17	5
KOKO Gmbh	DMS® base cream high classic	1028c18	5
KOKO Gmbh	DMS® base cream high classic	L042E18	5
KOKO Gmbh	DMS® base cream high classic	1053f18	3
KOKO Gmbh	DMS® base cream high classic	L050I18	5
KOKO GmbH	DMS® base cream high classic	L030L16	3
KOKO GmbH & Co. KG	DMS® base cream high classic	L054B16	1
Koko Gmbh	DMS® base cream high classic...	L035F17	1
KOKO GmbH & Co. KG	DMS® base cream high classic...	L018D16	1
Beiersdorf	Eucerinum O/W basis	24830308WA	1
Beiersdorf	Eucerinum O/W basis	319030108WA	1
Beiersdorf	Eucerinum O/W basis	61130108WA	1
Beiersdorf	Eucerinum O/W basis	8373038WA	1
Beiersdorf	Eucerinum O/W basis	84030108WA	1
Beiersdorf / Noweda	Eucerinum O/W basis	94830108WA	1
Beiersdorf AG	Eucerinum O/W basis	2483030308WA	1
Beiersdorf AG	Eucerinum O/W basis	24830308WA	1
Beiersdorf AG	Eucerinum O/W basis	64030208WA	1
Beiersdorf AG / Allianc...	Eucerinum O/W basis	64030208WA	1
Beiersdorf AG/ Alliance...	Eucerinum O/W basis	80230108WA	1
Beiersdorf AG/Kehr	Eucerinum O/W basis	84030108WA	2
Beiersdorf AG/Noweda	Eucerinum O/W basis	53430208WA	1
Beiersdorf/ Noweda	Eucerinum O/W basis	94830108WA	1
Beiersdorf/ Phoenix	Eucerinum O/W basis	80230108WA	1
Beiersdorf/ Phoenix	Eucerinum O/W basis	84030208WA	1
Beiersdorf/AHD	Eucerinum O/W basis	51630108WA	1
Beiersdorf/AHD	Eucerinum O/W basis	64030208WA	1

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Supplier	Substance	Batch	Spectra
Beiersdorf/Gehe	Eucerinum O/W basis	31930108WA	1
Beiersdorf/Gehe	Eucerinum O/W basis	80230108WA	1
Beiersdorf/Gehe	Eucerinum O/W basis	84030208WA	1
Beiersdorf/kehr	Eucerinum O/W basis	72630108WA	1
Beiersdorf/Kehr	Eucerinum O/W basis	53430208WA	3
Beiersdorf/Kehr	Eucerinum O/W basis	61130108WA	1
Beiersdorf/Kehr	Eucerinum O/W basis	84030108WA	3
Beiersdorf/Kehr	Eucerinum O/W basis	84030208WA	4
Beiersdorf/Kehr	Eucerinum O/W basis	94830108WA	4
Beiersdorf/VDL	Eucerinum O/W basis	64030208WA	1
Caelo	Eucerinum O/W basis	31930108WA	1
Caelo	Eucerinum O/W basis	64030208WA	1
Caelo	Eucerinum O/W basis	13730308WA	1
Allianz Healthcare	Eucerinum W/O basis	64030108wa	1
Caelo	Eucerinum W/O basis	53430208WA	4
Baiersdorf	Eucerinum W/O basis	24830208WA	1
Baiersdorf	Eucerinum W/O basis	41839108WA	1
Baiersdorf	Eucerinum W/O basis	43430208WA	1
BDF	Eucerinum W/O basis	31230108WA	1
BDF	Eucerinum W/O basis	41830108WA	1
BDF / Gehe	Eucerinum W/O basis	83730208WA	1
BDF / Noweda	Eucerinum W/O basis	43430208WA	1
BDF / Sanacorp	Eucerinum W/O basis	21430108WA	1
Beiersdor	Eucerinum W/O basis	541830108WA	1
beiersdorf	Eucerinum W/O basis	31230108WA	1
beiersdorf	Eucerinum W/O basis	24830208WA	1
beiersdorf	Eucerinum W/O basis	94930108	1
Beiersdorf	Eucerinum W/O basis	21430108WA	2
Beiersdorf	Eucerinum W/O basis	24830208WA	1
Beiersdorf	Eucerinum W/O basis	32930208WA	4
Beiersdorf	Eucerinum W/O basis	31230108wa	1
Beiersdorf	Eucerinum W/O basis	34930308WA	6
Beiersdorf	Eucerinum W/O basis	51630108WA	8
Beiersdorf	Eucerinum W/O basis	24072015A	1
Beiersdorf	Eucerinum W/O basis	516301328wa	1
Beiersdorf	Eucerinum W/O basis	438679	1
Beiersdorf	Eucerinum W/O basis	64030108WA	3
Beiersdorf	Eucerinum W/O basis	72630108WA	8
Beiersdorf	Eucerinum W/O basis	80339108WA	1
Beiersdorf	Eucerinum W/O basis	80330108WA	2
Beiersdorf	Eucerinum W/O basis	83730308WA	1
Beiersdorf	Eucerinum W/O basis	94930108	1
Beiersdorf	Eucerinum W/O basis	94930208	1
Beiersdorf / Alliance h...	Eucerinum W/O basis	72630108WA	1
Beiersdorf / Fiebig	Eucerinum W/O basis	72630108WA	1
Beiersdorf / Gehe	Eucerinum W/O basis	83730208WA	1
Beiersdorf / Noweda	Eucerinum W/O basis	83730208WA	1
Beiersdorf / Noweda	Eucerinum W/O basis	94930308	1
Beiersdorf / Phoenix	Eucerinum W/O basis	80330108WA	1
Beiersdorf / Phönix	Eucerinum W/O basis	53430208WA	1
Beiersdorf /AHC	Eucerinum W/O basis	83730208WA	1
Beiersdorf AG	Eucerinum W/O basis	32930208WA	3
Beiersdorf AG	Eucerinum W/O basis	34930308WA	1
Beiersdorf AG	Eucerinum W/O basis	41830108WA	1
Beiersdorf AG	Eucerinum W/O basis	51630108WA	6
Beiersdorf AG	Eucerinum W/O basis	64030108WA	1
Beiersdorf AG	Eucerinum W/O basis	72630108WA	1
Beiersdorf AG	Eucerinum W/O basis	80330108WA	6
Beiersdorf AG	Eucerinum W/O basis	83730208WA	1
Beiersdorf AG	Eucerinum W/O basis	53630108WA	1

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Supplier	Substance	Batch	Spectra
Beiersdorf AG	Eucerinum W/O basis	3730208WA	1
Beiersdorf AG / Gehe	Eucerinum W/O basis	83730208WA	2
Beiersdorf AG / Gehe	Eucerinum W/O basis	83730308WA	1
Beiersdorf AG/Noweda	Eucerinum W/O basis	31230108WA	1
Beiersdorf Manufacturin...	Eucerinum W/O basis	83730208WA	1
Beiersdorf/ Gehe	Eucerinum W/O basis	80330108WA	1
Beiersdorf/ Phoenix	Eucerinum W/O basis	64030108WA	1
Beiersdorf/ Sanacorp	Eucerinum W/O basis	418301087WA	1
Beiersdorf/ Vedono	Eucerinum W/O basis	34930308WA	1
Beiersdorf/Alliance	Eucerinum W/O basis	72630108WA	1
Beiersdorf/Alliance	Eucerinum W/O basis	94930108	1
Beiersdorf/Alliance Hea...	Eucerinum W/O basis	72630108WA	1
Beiersdorf/Anzag	Eucerinum W/O basis	31230108WA	1
Beiersdorf/E&J	Eucerinum W/O basis	80330108WA	1
Beiersdorf/Gehe	Eucerinum W/O basis	43430208WA	1
Beiersdorf/Gehe	Eucerinum W/O basis	64030108WA	1
Beiersdorf/Gehe	Eucerinum W/O basis	80330108WA	1
Beiersdorf/Gehe	Eucerinum W/O basis	83730208WA	1
Beiersdorf/Gehe	Eucerinum W/O basis	83730308WA	2
Beiersdorf/Gehe	Eucerinum W/O basis	94930208	1
Beiersdorf/Geibo	Eucerinum W/O basis	94930108	1
Beiersdorf/Jenne	Eucerinum W/O basis	94930108	1
Beiersdorf/Kehr	Eucerinum W/O basis	64030108WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	34930308WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	41830108Wa	1
Beiersdorf/Noweda	Eucerinum W/O basis	41830108WA	2
Beiersdorf/Noweda	Eucerinum W/O basis	51630108WA	6
Beiersdorf/Noweda	Eucerinum W/O basis	51630108wa	1
Beiersdorf/Noweda	Eucerinum W/O basis	53430208WA	7
Beiersdorf/Noweda	Eucerinum W/O basis	64030108WA	2
Beiersdorf/Noweda	Eucerinum W/O basis	72630108VVA	1
Beiersdorf/Noweda	Eucerinum W/O basis	72630108WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	726300108WA	1
Beiersdorf/Noweda	Eucerinum W/O basis	80330108WA	2
Beiersdorf/Noweda	Eucerinum W/O basis	83730208WA	2
Beiersdorf/Noweda	Eucerinum W/O basis	94930108	1
Beiersdorf/Noweda	Eucerinum W/O basis	94930208	1
Beiersdorf/Phoenix	Eucerinum W/O basis	34930308WA	1
Beiersdorf/Phoenix	Eucerinum W/O basis	51630108WA	1
Beiersdorf/Phönix	Eucerinum W/O basis	53430208WA	1
Beiersdorf/Phönix	Eucerinum W/O basis	80330108WA	2
Beiersdorf/Phönix	Eucerinum W/O basis	83730208WA	2
Beiersdorf/Phönix	Eucerinum W/O basis	94930208	1
Beiersdorf/Sanacorp	Eucerinum W/O basis	31230108WA	1
BeiersdorfPhoenix	Eucerinum W/O basis	31230108WA	1
Caelo	Eucerinum W/O basis	51630108wa	1
Caelo	Eucerinum W/O basis	41830108WA	3
Caelo	Eucerinum W/O basis	21430108WA	1
Caelo	Eucerinum W/O basis	72630108WA	1
Caelo	Eucerinum W/O basis	72630108Wa	1
Caelo	Eucerinum W/O basis	51630108WA	2
Caelo	Eucerinum W/O basis	51630108	1
eucerinum	Eucerinum W/O basis	41830108WA	1
Fiebig	Eucerinum W/O basis	80330108WA	1
Gehe	Eucerinum W/O basis	32930208WA	1
Gehe/Beiersdorf	Eucerinum W/O basis	51630108WA	1
Caelo	Eucerinum W/O basis	64030108WA	2
Geibo/ Beiersdorf	Eucerinum W/O basis	72630108WA	1
Geibo/ Beiersdorf	Eucerinum W/O basis	83730308WA	1
Geibo/Beiersdorf	Eucerinum W/O basis	83730208WA	1

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Supplier	Substance	Batch	Spectra
Geibo/Beiersdorf	Eucerinum W/O basis	83730308WA	1
Ichthyol-Gesellschaft	Eucerinum W/O basis	80330108WA	1
Noweda	Eucerinum W/O basis	72630108WA	4
Noweda	Eucerinum W/O basis	83730208WA	2
Noweda	Eucerinum W/O basis	8373C208WA	1
Noweda	Eucerinum W/O basis	83730308WA	1
Noweda	Eucerinum W/O basis	94930208	1
Noweda	Eucerinum W/O basis	94930108	2
Noweda/BDF	Eucerinum W/O basis	51630108WA	1
Noweda/Beiersdorf	Eucerinum W/O basis	83730308WA	1
Ph.Eur.8.0	Eucerinum W/O basis	41830108WA	1
Phoenix	Eucerinum W/O basis	94930208	1
Phönix	Eucerinum W/O basis	94930108	1
Rondell Apotheke	Eucerinum W/O basis	51630108WA	1
Sanacorp	Eucerinum W/O basis	80330108WA	1
Sanacorp/Beiersdorf	Eucerinum W/O basis	80330108WA	3
Sanacorp/Beiersdorf	Eucerinum W/O basis	94930108	1
AHD	Excipial® hydro cream	R011	1
Alliance/Spirig	Excipial® hydro cream	NO43	1
Caelo	Excipial® hydro cream	LOT50782	1
Caelo	Excipial® hydro cream	V031	1
Caelo	Excipial® hydro cream	V071	2
Caelo	Excipial® hydro cream	R045	1
Chiesi/Phoenix	Excipial® hydro cream	LOTV071	1
Fa.Gehe	Excipial® hydro cream	20160727Ma3	1
Galderma	Excipial® hydro cream	S054	1
Galderma	Excipial® hydro cream	T052	4
Galderma	Excipial® hydro cream	S041	1
Galderma	Excipial® hydro cream	LOTV071	2
Galderma	Excipial® hydro cream	LOTV051	1
Galderma	Excipial® hydro cream	V051	2
Galderma	Excipial® hydro cream	LOTV072	1
Galderma	Excipial® hydro cream	50634	2
Galderma	Excipial® hydro cream	50782	3
Galderma	Excipial® hydro cream	50564	1
Galderma	Excipial® hydro cream	LOT50782	1
Galderma /	Excipial® hydro cream	P28013-0	1
Galderma / Noweda	Excipial® hydro cream	T052	1
Galderma /Phönix	Excipial® hydro cream	LOTT052	2
Galderma/	Excipial® hydro cream	S012	1
Galderma/	Excipial® hydro cream	V011	1
Galderma/	Excipial® hydro cream	VO11	1
Galderma/ Gehe	Excipial® hydro cream	V051	1
Galderma/ Sana	Excipial® hydro cream	S025	1
Galderma/ Sana	Excipial® hydro cream	S024	1
Galderma/Alliance Healt…	Excipial® hydro cream	SO25	1
Galderma/Ebert	Excipial® hydro cream	VO41	1
Galderma/Galderma	Excipial® hydro cream	S024	2
Galderma/Galderma	Excipial® hydro cream	so25	1
Galderma/Galderma	Excipial® hydro cream	S054	1
Galderma/Galderma	Excipial® hydro cream	V051	1
Galderma/Galderma	Excipial® hydro cream	V042	1
Galderma/Gehe	Excipial® hydro cream	R031	1
Galderma/Gehe	Excipial® hydro cream	V042	1
Galderma/Gehe	Excipial® hydro cream	V071	1
Galderma/Gehe	Excipial® hydro cream	V072	2
Galderma/Gehe	Excipial® hydro cream	8767001	1
Galderma/Gehe	Excipial® hydro cream	9767001	1
Galderma/Noweda	Excipial® hydro cream	S054	2
Galderma/Noweda	Excipial® hydro cream	170420EH/LOTT012	1

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Supplier	Substance	Batch	Spectra
Galderma/Noweda	Excipial® hydro cream	170706EH/LOTT091	1
Galderma/Noweda	Excipial® hydro cream	V042	1
Galderma/Noweda	Excipial® hydro cream	V051	2
Galderma/Noweda	Excipial® hydro cream	180319EH/LOTV051	1
Galderma/Phoenix	Excipial® hydro cream	V031	1
Galderma/Phönic	Excipial® hydro cream	VO61	1
Galderma/Phönix	Excipial® hydro cream	S045	1
Galderma/Phönix	Excipial® hydro cream	S013	1
Galderma/Phönix	Excipial® hydro cream	V011	2
Galderma/Phönix	Excipial® hydro cream	V071	1
Galderma/Phönix	Excipial® hydro cream	50235	1
Galderma/Phönix	Excipial® hydro cream	50782	4
Galderma/Phönix	Excipial® hydro cream	50515	1
Galderma/Phönix	Excipial® hydro cream	9767005	1
Galderma/Sanacorp	Excipial® hydro cream	LOTV041	1
Galderma/Würmi	Excipial® hydro cream	R031	1
Galderma/Würmtal-APO	Excipial® hydro cream	S041	1
Galderma-Spirig	Excipial® hydro cream	To52-20171127Ma11	1
Galderma-Spirig	Excipial® hydro cream	V041-20180619Ma8	1
Galderma-Spirig	Excipial® hydro cream	50235-E20190115Ma10	1
Galderma-Spirig,Gehe 14. . .	Excipial® hydro cream	V061-20180830Ma11	1
Gehe,Galderma Spirig	Excipial® hydro cream	R031-20160615Ma7	1
Gladerma/Ebert	Excipial® hydro cream	VO72	1
Jenne	Excipial® hydro cream	S041	1
Noweda	Excipial® hydro cream	1120114	1
Noweda	Excipial® hydro cream	VO51	1
Noweda/Galderma	Excipial® hydro cream	TO91	2
Phoenix/Galderma	Excipial® hydro cream	TO12	1
Phoenix/Spirig	Excipial® hydro cream	M015	1
Phoenix/Spirig	Excipial® hydro cream	N044	1
Phönix	Excipial® hydro cream	V011	1
Phönix/Galderma	Excipial® hydro cream	9767005	1
Phönix/Spirig	Excipial® hydro cream	N034	1
Römerapo.	Excipial® hydro cream	R011	2
Sanacorp	Excipial® hydro cream	LOTN011	1
Sanacorp	Excipial® hydro cream	N011	1
Spierig Pharma AG/ Anzag	Excipial® hydro cream	LOTNO34	1
Spierig Pharma AG/ Anzag	Excipial® hydro cream	LOTR013	1
Spierig/Gehe	Excipial® hydro cream	R014	1
spirig	Excipial® hydro cream	M014	2
spirig	Excipial® hydro cream	813993/10	1
spirig	Excipial® hydro cream	M041	6
spirig	Excipial® hydro cream	MO34	1
spirig	Excipial® hydro cream	N034	2
spirig	Excipial® hydro cream	No14	1
spirig	Excipial® hydro cream	N043	2
spirig	Excipial® hydro cream	R013	2
spirig	Excipial® hydro cream	N045	2
spirig	Excipial® hydro cream	R014	2
spirig	Excipial® hydro cream	s025	1
Spirig	Excipial® hydro cream	K013	1
Spirig	Excipial® hydro cream	NO35	1
Spirig	Excipial® hydro cream	N043	1
Spirig	Excipial® hydro cream	R013	1
Spirig	Excipial® hydro cream	S025	6
Spirig (Galderma)	Excipial® hydro cream	TO12	2
Spirig (Galderma)	Excipial® hydro cream	TO11	1
Spirig (Galderma)	Excipial® hydro cream	V011	2
Spirig / Anzag	Excipial® hydro cream	813993/09	1
Spirig / Anzag	Excipial® hydro cream	813993/10	1

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Supplier	Substance	Batch	Spectra
Spirig / Anzag	Excipial® hydro cream	N034	1
Spirig / Anzag	Excipial® hydro cream	LOTN043	1
Spirig / Gehe	Excipial® hydro cream	N011	1
Spirig / Noweda	Excipial® hydro cream	N035	1
Spirig /Gehe	Excipial® hydro cream	LOTN044	1
Spirig Pharma	Excipial® hydro cream	N013	1
Spirig Pharma	Excipial® hydro cream	813993/10	1
Spirig Pharma	Excipial® hydro cream	N011	1
Spirig Pharma	Excipial® hydro cream	LON014	1
Spirig Pharma	Excipial® hydro cream	N044	1
Spirig Pharma AG	Excipial® hydro cream	813993/12	1
Spirig Pharma AG	Excipial® hydro cream	R025	5
Spirig Pharma AG/GEHE	Excipial® hydro cream	R011	1
Spirig Pharma/ G	Excipial® hydro cream	S053	1
Spirig Pharma/ Noweda	Excipial® hydro cream	N042	2
Spirig/Anzag	Excipial® hydro cream	LOTM041	1
Spirig/Anzag	Excipial® hydro cream	N035	1
Spirig/Fiebig	Excipial® hydro cream	N013	1
Spirig/Gehe	Excipial® hydro cream	M012	1
Spirig/Gehe	Excipial® hydro cream	LOTR031	2
Spirig/Noweda	Excipial® hydro cream	N043	3
Spirig/Phönix	Excipial® hydro cream	R013	1
Spirig/Phönix	Excipial® hydro cream	R014	1
Spririg / Noweda	Excipial® hydro cream	S041	5
Alliance Healthcare	Excipial® lipo cream	M045	1
Anzag/ Chiesi	Excipial® lipo cream	LOTR012	2
Caelo	Excipial® lipo cream	V051	1
Caelo	Excipial® lipo cream	9031	1
Caelo	Excipial® lipo cream	7121	1
galderma	Excipial® lipo cream	LOT50627	1
Galderma	Excipial® lipo cream	N061	2
Galderma	Excipial® lipo cream	R026	2
Galderma	Excipial® lipo cream	RO12	1
Galderma	Excipial® lipo cream	R042	1
Galderma	Excipial® lipo cream	R035	2
Galderma	Excipial® lipo cream	LOTS032	1
Galderma	Excipial® lipo cream	T021	2
Galderma	Excipial® lipo cream	T061	2
Galderma	Excipial® lipo cream	v042	1
Galderma	Excipial® lipo cream	LOTV041	1
Galderma	Excipial® lipo cream	V091	1
Galderma	Excipial® lipo cream	50567	1
Galderma	Excipial® lipo cream	8769004	1
Galderma	Excipial® lipo cream	9769004	1
Galderma	Excipial® lipo cream	9769010	1
Galderma /AHD	Excipial® lipo cream	50567	3
Galderma /AHD	Excipial® lipo cream	8769004	1
Galderma/	Excipial® lipo cream	9769004	1
Galderma/ Fiebig	Excipial® lipo cream	LOTV111	1
Galderma/ Noweda	Excipial® lipo cream	s023	6
Galderma/ Noweda	Excipial® lipo cream	S031	9
Galderma/ Noweda	Excipial® lipo cream	t022	5
Galderma/ Noweda	Excipial® lipo cream	T022	4
Galderma/ Noweda	Excipial® lipo cream	T021	5
Galderma/ Sanacorp	Excipial® lipo cream	LOT50567	1
Galderma/ Sanacorp	Excipial® lipo cream	50567	1
Galderma/ Sanacorp	Excipial® lipo cream	8769004	1
Galderma/AHCA	Excipial® lipo cream	9769004	1
Galderma/Alliance	Excipial® lipo cream	T061	1
Galderma/Alliance	Excipial® lipo cream	V091	2

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Supplier	Substance	Batch	Spectra
Galderma/Alliance	Excipial® lipo cream	V112	1
Galderma/Alliance	Excipial® lipo cream	769002	1
Galderma/Alliance	Excipial® lipo cream	769013	2
Galderma/Anzag	Excipial® lipo cream	S011	1
Galderma/Galderma	Excipial® lipo cream	RO26	1
Galderma/Galderma	Excipial® lipo cream	ro26	1
Galderma/Galderma	Excipial® lipo cream	R042	9
Galderma/Galderma	Excipial® lipo cream	S023	8
Galderma/Galderma	Excipial® lipo cream	T021	8
Galderma/Galderma	Excipial® lipo cream	V121	1
Galderma/Galderma	Excipial® lipo cream	50567	1
Galderma/Galderma	Excipial® lipo cream	8769004	1
Galderma/Gehe	Excipial® lipo cream	R042	2
Galderma/Gehe	Excipial® lipo cream	V091	1
Galderma/Gehe	Excipial® lipo cream	50849	1
Galderma/Noweda	Excipial® lipo cream	R026	2
Galderma/Noweda	Excipial® lipo cream	R011	1
Galderma/Noweda	Excipial® lipo cream	170420EL/LOTT021	1
Galderma/Noweda	Excipial® lipo cream	T021	1
Galderma/Noweda	Excipial® lipo cream	171819E/LOTT021	1
Galderma/Noweda	Excipial® lipo cream	180208L/LOTV091	1
Galderma/Noweda	Excipial® lipo cream	50567	1
Galderma/Phönix	Excipial® lipo cream	R042	1
Galderma/Phönix	Excipial® lipo cream	R026	2
Galderma/Phönix	Excipial® lipo cream	R012	1
Galderma/Phönix	Excipial® lipo cream	S031	1
Galderma/Phönix	Excipial® lipo cream	S023	1
Galderma/Phönix	Excipial® lipo cream	S032	1
Galderma/Phönix	Excipial® lipo cream	T021	1
Galderma/Phönix	Excipial® lipo cream	50627	1
Galderma/Phönix	Excipial® lipo cream	50567	6
Galderma/Phönix	Excipial® lipo cream	9769004	3
Galderma/Phönix	Excipial® lipo cream	8769004	1
Galderma/Phönix	Excipial® lipo cream	9769011	6
Galderma/Phönix	Excipial® lipo cream	9769010	1
Galderma/Phönix WE: 03…	Excipial® lipo cream	LOTV012	1
Galderma/Würmtalapo	Excipial® lipo cream	R042	2
Galmeda Noweda	Excipial® lipo cream	180504EL/LOTV112	1
Gehe	Excipial® lipo cream	N061	1
Gehe/Galderma	Excipial® lipo cream	LOTS031	1
Noweda	Excipial® lipo cream	50627	1
Noweda	Excipial® lipo cream	9769030	1
Noweda/ Galderma	Excipial® lipo cream	V112180607EL	1
Caelo	Excipial® lipo cream	LOTSo23	1
Phoenix/Galderma	Excipial® lipo cream	50567	1
Phönix/Galderma	Excipial® lipo cream	SO23	1
Sanacorp	Excipial® lipo cream	MO27	1
Sanacorp	Excipial® lipo cream	LOTN016	1
spirig	Excipial® lipo cream	M016	4
spirig	Excipial® lipo cream	M017	1
spirig	Excipial® lipo cream	813994/09	1
spirig	Excipial® lipo cream	M042	2
spirig	Excipial® lipo cream	N018	4
spirig	Excipial® lipo cream	N021	5
spirig	Excipial® lipo cream	R012	3
spirig	Excipial® lipo cream	N061	3
spirig	Excipial® lipo cream	r042	1
Spirig	Excipial® lipo cream	K021	1
Spirig	Excipial® lipo cream	N021	1
Spirig	Excipial® lipo cream	R012	4

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Supplier	Substance	Batch	Spectra
Spirig (Galderma)	Excipial® lipo cream	T061	1
Spirig / Anzag	Excipial® lipo cream	M017	1
Spirig / Anzag	Excipial® lipo cream	813994/09	1
Spirig / Anzag	Excipial® lipo cream	M042	3
Spirig / Anzag	Excipial® lipo cream	N018	3
Spirig / Anzag	Excipial® lipo cream	NO18	1
Spirig / Anzag	Excipial® lipo cream	LOTNO21	2
Spirig /Gehe	Excipial® lipo cream	LOTRO12	1
Spirig /Gehe	Excipial® lipo cream	LOTNO21	2
Spirig /Gehe	Excipial® lipo cream	RO12	1
Spirig Pharma	Excipial® lipo cream	813994/09	2
Spirig Pharma	Excipial® lipo cream	T021	1
Spirig Pharma AG	Excipial® lipo cream	M042	1
Spirig Pharma AG/Allian...	Excipial® lipo cream	N018	1
Spirig Pharma AG/GEHE	Excipial® lipo cream	R012	1
Spirig Pharma Europe GmbH	Excipial® lipo cream	R026	1
Spirig/AHD	Excipial® lipo cream	M041	2
Spirig/AHD	Excipial® lipo cream	M017	1
Spirig/AHD	Excipial® lipo cream	N018	2
Spirig/AHD	Excipial® lipo cream	V112	3
Spirig/Anzag	Excipial® lipo cream	S023	1
Spirig/Anzag	Excipial® lipo cream	S031	1
Spirig/Anzag	Excipial® lipo cream	R011	1
Spirig/Gehe	Excipial® lipo cream	R012	1
Spirig/Gehe	Excipial® lipo cream	R026	1
Spirig/Otto	Excipial® lipo cream	50627	1
Spirig/Phoenix	Excipial® lipo cream	M042	2
Spirig/Phönix	Excipial® lipo cream	4622	1
Spirig/Phönix	Excipial® lipo cream	R012	2
Spirig/Phönix	Excipial® lipo cream	R042	1
Wolff	Excipial® lipo cream	S031	1
Caelo	Excipial® U Lipolotio	R186	1
Caelo	Excipial® U Lipolotio	V101	1
Caelo	Excipial® U Lipolotio	V143	1
Caelo	Excipial® U Lipolotio	S206	1
Caelo	Excipial® U Lipolotio	LotV137	1
Caelo	Excipial® U Lipolotio	R167	1
Caelo	Excipial® U Lipolotio	LoTV143	1
Caelo	Excipial® U Lipolotio	173048	2
Caelo	Excipial® U Lipolotio	S073	1
Caesar & Loretz GmbH	Excipial® U Lipolotio	19065102	1
Dermapharm	Excipial® U Lipolotio	169010	1
Euro/ Phönix	Excipial® U Lipolotio	4417A-03749	1
Fagron	Excipial® U Lipolotio	N168	2
Fagron	Excipial® U Lipolotio	V081	1
Fiebig	Excipial® U Lipolotio	T061	2
Fiebig/DR.Wolf	Excipial® U Lipolotio	V028	1
Fischar	Excipial® U Lipolotio	LOTNO85	1
Galaderma	Excipial® U Lipolotio	R072	1
Galaderma/Krieger	Excipial® U Lipolotio	VO11	1
Galaderma/Krieger	Excipial® U Lipolotio	LOT50249	1
Galaderma/Krieger	Excipial® U Lipolotio	LOT50842	1
Galaderma/Krieger	Excipial® U Lipolotio	174756	1
Galaderma/Krieger	Excipial® U Lipolotio	173469	1
Galaderma/Krieger	Excipial® U Lipolotio	303485	1
Galaderma/Krieger	Excipial® U Lipolotio	318718	1
Galaderma/Krieger	Excipial® U Lipolotio	309994	1
Galaderma/Krieger	Excipial® U Lipolotio	318628	1
Galaderma/Phönix	Excipial® U Lipolotio	V041	1
Galaderma/Phönix	Excipial® U Lipolotio	LOTV152	1

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Supplier	Substance	Batch	Spectra
galderma	Excipial® U Lipolotio	R024	1
Galderma	Excipial® U Lipolotio	R111	1
Galderma	Excipial® U Lipolotio	R167	2
Galderma	Excipial® U Lipolotio	R168	1
Galderma	Excipial® U Lipolotio	S064	1
Galderma	Excipial® U Lipolotio	S091	1
Galderma	Excipial® U Lipolotio	R171	1
Galderma	Excipial® U Lipolotio	R172	1
Galderma	Excipial® U Lipolotio	S137	1
Galderma	Excipial® U Lipolotio	S147	1
Galderma	Excipial® U Lipolotio	T056	1
Galderma	Excipial® U Lipolotio	LOTS123	1
Galderma	Excipial® U Lipolotio	T125	1
Galderma	Excipial® U Lipolotio	S148	1
Galderma	Excipial® U Lipolotio	LOTV121	1
Galderma	Excipial® U Lipolotio	V139	2
Galderma	Excipial® U Lipolotio	V153	2
Galderma	Excipial® U Lipolotio	V159	1
Galderma	Excipial® U Lipolotio	V053	1
Galderma	Excipial® U Lipolotio	50458	1
Galderma	Excipial® U Lipolotio	V101	1
Galderma	Excipial® U Lipolotio	V152	1
Galderma	Excipial® U Lipolotio	50688	1
Galderma	Excipial® U Lipolotio	50346	1
Galderma	Excipial® U Lipolotio	50852	6
Galderma	Excipial® U Lipolotio	270918A	1
Galderma	Excipial® U Lipolotio	169853	2
Galderma	Excipial® U Lipolotio	169005	1
Galderma	Excipial® U Lipolotio	170615	1
Galderma	Excipial® U Lipolotio	173469	2
Galderma	Excipial® U Lipolotio	174756	1
Galderma	Excipial® U Lipolotio	305489	2
Galderma	Excipial® U Lipolotio	310709	1
Galderma	Excipial® U Lipolotio	308637	1
Galderma	Excipial® U Lipolotio	311839	1
Galderma (Spirig Pharma…	Excipial® U Lipolotio	R061	1
Galderma (Spirig Pharma…	Excipial® U Lipolotio	T057	1
Galderma / Noweda	Excipial® U Lipolotio	V152	1
Galderma / Noweda	Excipial® U Lipolotio	T115	1
Galderma / Galderma	Excipial® U Lipolotio	R086	1
Galderma / Kehr	Excipial® U Lipolotio	R171	1
Galderma / Kehr	Excipial® U Lipolotio	R167	1
Galderma / Kehr	Excipial® U Lipolotio	T029	2
Galderma / Kehr	Excipial® U Lipolotio	T156	2
Galderma / Noweda	Excipial® U Lipolotio	T073/170522EUL	1
Galderma /AHD	Excipial® U Lipolotio	169853	1
Galderma /Fiebig	Excipial® U Lipolotio	170615	2
Galderma Labor.	Excipial® U Lipolotio	169010	1
Galderma Labor.	Excipial® U Lipolotio	169110	1
Galderma Labor.	Excipial® U Lipolotio	310709	2
Galderma Labor.	Excipial® U Lipolotio	312811	1
Galderma, Sanacorp	Excipial® U Lipolotio	LOTS042	1
Galderma/	Excipial® U Lipolotio	319921	1
Galderma/ Alliance	Excipial® U Lipolotio	T115	1
Galderma/ Fiebig	Excipial® U Lipolotio	830071/17	1
Galderma/ Noweda	Excipial® U Lipolotio	LOT50450	1
Galderma/ NOWEDA	Excipial® U Lipolotio	V082	1
Galderma/AEP	Excipial® U Lipolotio	V165	1
Galderma/Alliance Healt…	Excipial® U Lipolotio	T121	1
Galderma/Anzag	Excipial® U Lipolotio	R183	1

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Supplier	Substance	Batch	Spectra
Galderma/Anzag	Excipial® U Lipolotio	S206	1
Galderma/Fiebig	Excipial® U Lipolotio	319844	2
galderma/G	Excipial® U Lipolotio	LOTS202	1
Galderma/Galderma	Excipial® U Lipolotio	s017	1
Galderma/Galderma	Excipial® U Lipolotio	S017	1
Galderma/Galderma	Excipial® U Lipolotio	S142	1
Galderma/Galderma	Excipial® U Lipolotio	50852	1
Galderma/Galderma	Excipial® U Lipolotio	174960	1
Galderma/Gehe	Excipial® U Lipolotio	R189	1
Galderma/Gehe	Excipial® U Lipolotio	T061	1
Galderma/Gehe	Excipial® U Lipolotio	T066	1
Galderma/Gehe	Excipial® U Lipolotio	S139	1
Galderma/Gehe	Excipial® U Lipolotio	T156	2
Galderma/Gehe	Excipial® U Lipolotio	V108	1
Galderma/Gehe	Excipial® U Lipolotio	LOT50450	1
Galderma/Gehe	Excipial® U Lipolotio	50450	1
Galderma/Gehe	Excipial® U Lipolotio	50691	1
Galderma/Gehe	Excipial® U Lipolotio	50842	1
Galderma/Gehe	Excipial® U Lipolotio	171710	1
Galderma/Gehe	Excipial® U Lipolotio	169831	1
Galderma/Gehe	Excipial® U Lipolotio	312417	1
Galderma/Gehe	Excipial® U Lipolotio	332540	1
Galderma/Graf-Eberhard-...	Excipial® U Lipolotio	174966	1
Galderma/Graf-Eberhard-...	Excipial® U Lipolotio	310709	1
Galderma/Kehr	Excipial® U Lipolotio	S071	1
Galderma/Kehr	Excipial® U Lipolotio	S203	1
Galderma/Kehr	Excipial® U Lipolotio	320973	1
Galderma/Noweda	Excipial® U Lipolotio	170420EUL/LOTS204	1
Galderma/Noweda	Excipial® U Lipolotio	170518EUL/LOTT073	1
Galderma/Noweda	Excipial® U Lipolotio	170316EL/LOTT073	1
Galderma/Noweda	Excipial® U Lipolotio	V011	1
Galderma/Noweda	Excipial® U Lipolotio	V041	1
Galderma/Noweda	Excipial® U Lipolotio	170906EL/T072	1
Galderma/Noweda	Excipial® U Lipolotio	V141	1
Galderma/Noweda	Excipial® U Lipolotio	50689	2
Galderma/Noweda	Excipial® U Lipolotio	50842	1
Galderma/Noweda	Excipial® U Lipolotio	V082	1
Galderma/Noweda	Excipial® U Lipolotio	V143	1
Galderma/Noweda	Excipial® U Lipolotio	314142	1
Galderma/Noweda	Excipial® U Lipolotio	319844	1
Galderma/Noweda	Excipial® U Lipolotio	320973	1
Galderma/phoenix	Excipial® U Lipolotio	169010	1
Galderma/phoenix	Excipial® U Lipolotio	169847	1
Galderma/phoenix	Excipial® U Lipolotio	171711	3
Galderma/phoenix	Excipial® U Lipolotio	310709	5
Galderma/Phoenix	Excipial® U Lipolotio	LOTT085	1
Galderma/Phoenix	Excipial® U Lipolotio	3717E-03749	1
Galderma/Phoenix	Excipial® U Lipolotio	V041	1
Galderma/Phoenix	Excipial® U Lipolotio	V061	1
Galderma/Phoenix	Excipial® U Lipolotio	VO11	1
Galderma/Phoenix	Excipial® U Lipolotio	50450	1
Galderma/Phoenix	Excipial® U Lipolotio	175042	2
Galderma/Phoenix	Excipial® U Lipolotio	308637	2
Galderma/Phoenix	Excipial® U Lipolotio	312417	2
Galderma/Phoenix	Excipial® U Lipolotio	314603	2
Galderma/Phoenix	Excipial® U Lipolotio	319422	3
Galderma/Phoenix	Excipial® U Lipolotio	319748	1
Galderma/Phönix	Excipial® U Lipolotio	T116	1
Galderma/Phönix	Excipial® U Lipolotio	V041	2
Galderma/Phönix	Excipial® U Lipolotio	V136	1

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Supplier	Substance	Batch	Spectra
Galderma/Phönix	Excipial® U Lipolotio	50876	1
Galderma/Phönix	Excipial® U Lipolotio	50569	1
Galderma/Phönix	Excipial® U Lipolotio	170615	4
Galderma/Phönix	Excipial® U Lipolotio	173469	4
Galderma/Phönix	Excipial® U Lipolotio	314603	1
Galderma/Phönix	Excipial® U Lipolotio	319748	1
Galderma/Sanacorp	Excipial® U Lipolotio	V103	2
Galderma/Sanacorp	Excipial® U Lipolotio	V073	1
Galderma/Sanacorp	Excipial® U Lipolotio	V038	1
Galderma/Sanacorp	Excipial® U Lipolotio	V151	1
Galderma/Sanacorp	Excipial® U Lipolotio	319351	1
Galderma/Spirig Pharma AG	Excipial® U Lipolotio	LOTR187	1
Galderma/Würmtal Apotheke	Excipial® U Lipolotio	S132	2
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	R142	1
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	S071	4
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	S205	2
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	T149	1
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	V142	1
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	50852	1
Galderma/Würmtal-Apotheke	Excipial® U Lipolotio	169010	1
Dermapharm	Excipial® U Lipolotio	311839	1
Gehe	Excipial® U Lipolotio	S132	1
Gehe	Excipial® U Lipolotio	S143	1
Gehe	Excipial® U Lipolotio	V152	1
Gehe	Excipial® U Lipolotio	V121	1
GEHE	Excipial® U Lipolotio	50459	1
GEHE	Excipial® U Lipolotio	50688	1
GEHE	Excipial® U Lipolotio	50890	2
GEHE	Excipial® U Lipolotio	174996	1
GEHE	Excipial® U Lipolotio	174966	1
GEHE	Excipial® U Lipolotio	309197	2
GEHE	Excipial® U Lipolotio	312811	1
Caelo	Excipial® U Lipolotio	LOTS081	1
Gehe/Galderma	Excipial® U Lipolotio	LotV011	1
GEHE/GALDERMA 25_11:16	Excipial® U Lipolotio	S147	1
Gehe-Spring	Excipial® U Lipolotio	LOTR167	1
Kehr/Galderma	Excipial® U Lipolotio	TO29	1
Nestle skin health	Excipial® U Lipolotio	174966	1
Nestle Skin Health	Excipial® U Lipolotio	174756	1
Nestle Skin Health/ Now…	Excipial® U Lipolotio	314142	1
Nestle Skin Health/Gehe	Excipial® U Lipolotio	174756	1
Nestle Skin Health/Noweda	Excipial® U Lipolotio	305489	2
Nestle Skin Health/Phönix	Excipial® U Lipolotio	303485	1
Nestle Skin Health/Phönix	Excipial® U Lipolotio	311839	1
Nestle Skin Health/Sana…	Excipial® U Lipolotio	319344	1
Noweda	Excipial® U Lipolotio	R261	1
Noweda	Excipial® U Lipolotio	305489	1
Noweda	Excipial® U Lipolotio	311839	2
Noweda	Excipial® U Lipolotio	319844	1
Noweda	Excipial® U Lipolotio	312811	2
Noweda	Excipial® U Lipolotio	327343	1
Caelo	Excipial® U Lipolotio	50569	1
Noweda/Galderma	Excipial® U Lipolotio	V121	1
Phoenix	Excipial® U Lipolotio	N105	1
Phoenix	Excipial® U Lipolotio	S091	1
Phoenix	Excipial® U Lipolotio	S138	2
Phoenix	Excipial® U Lipolotio	S148	1
Phoenix	Excipial® U Lipolotio	319748	1
Phoenix/Spirig	Excipial® U Lipolotio	N041	1
PHÖNIX	Excipial® U Lipolotio	T063	1

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Supplier	Substance	Batch	Spectra
PHÖNIX	Excipial® U Lipolotio	V039	1
PHÖNIX	Excipial® U Lipolotio	V105	1
sanacorp / Nestle	Excipial® U Lipolotio	174800	1
Sanacorp WE 25.02.17 -1…	Excipial® U Lipolotio	LOTS122	2
Spirg	Excipial® U Lipolotio	NO86	1
spirig	Excipial® U Lipolotio	M142	1
spirig	Excipial® U Lipolotio	NO13	1
spirig	Excipial® U Lipolotio	N058	3
spirig	Excipial® U Lipolotio	NO86	1
spirig	Excipial® U Lipolotio	R037	1
Spirig	Excipial® U Lipolotio	M091	1
Spirig	Excipial® U Lipolotio	N123	1
Spirig	Excipial® U Lipolotio	R047	1
Spirig	Excipial® U Lipolotio	LOTTO57	1
Spirig	Excipial® U Lipolotio	50450	1
Spirig	Excipial® U Lipolotio	169838	1
Spirig / Anzag	Excipial® U Lipolotio	M182	1
Spirig / Anzag	Excipial® U Lipolotio	NO32	1
Spirig / Anzag	Excipial® U Lipolotio	NO41	1
Spirig / Galderma / Anzag	Excipial® U Lipolotio	170615	1
Spirig / Galderma / Anzag	Excipial® U Lipolotio	169010	1
Spirig / Sanacorp	Excipial® U Lipolotio	R041	1
Spirig Pharma	Excipial® U Lipolotio	LOTK131	1
Spirig Pharma	Excipial® U Lipolotio	LOTNO13	1
Spirig Pharma	Excipial® U Lipolotio	M134	1
Spirig Pharma	Excipial® U Lipolotio	S122	1
Spirig Pharma	Excipial® U Lipolotio	V082	1
Spirig Pharma	Excipial® U Lipolotio	V053	1
Spirig Pharma	Excipial® U Lipolotio	V141	2
Spirig Pharma / Noweda	Excipial® U Lipolotio	S141	1
Spirig/ Noweda	Excipial® U Lipolotio	S225	1
Spirig/AHD	Excipial® U Lipolotio	M085	1
Spirig/AHD	Excipial® U Lipolotio	lotno86	1
Spirig/AHD	Excipial® U Lipolotio	N058	1
Spirig/Fiebig	Excipial® U Lipolotio	S143	1
Spirig/Galderma	Excipial® U Lipolotio	R156	2
Spirig/Galderma	Excipial® U Lipolotio	R146	1
Spirig/Gehe	Excipial® U Lipolotio	M102	2
Spirig/Gehe	Excipial® U Lipolotio	M182	1
Spirig/Gehe	Excipial® U Lipolotio	M146	1
Spirig/Gehe	Excipial® U Lipolotio	R114	1
Spirig/Gehe	Excipial® U Lipolotio	R262	1
Spirig/Kehr	Excipial® U Lipolotio	V038	1
Spirig/Noweda	Excipial® U Lipolotio	NO61	1
Spirig/Phönix	Excipial® U Lipolotio	R033	1
Spirig/Würmtal-Apotheke	Excipial® U Lipolotio	R145	2
Sprig (Galderma)/ G	Excipial® U Lipolotio	S123	1
Galaderma/Krieger	Excipial® U10 Lipolotio	T071	1
Galderma	Excipial® U10 Lipolotio	LOT50679	1
Galderma	Excipial® U10 Lipolotio	304231	1
Galderma/AHCA	Excipial® U10 Lipolotio	LOT50604	1
Galderma/Alliance	Excipial® U10 Lipolotio	T042	1
Galderma/Galderma	Excipial® U10 Lipolotio	308310	1
Galderma/Sanacorp	Excipial® U10 Lipolotio	V092	1
Galderma/Sanacorp	Excipial® U10 Lipolotio	169759	2
Galderma/Sanacorp	Excipial® U10 Lipolotio	50679	1
Galderma/Sanacorp	Excipial® U10 Lipolotio	308601	3
Galderma/Sanacorp	Excipial® U10 Lipolotio	320154	1
Galderma/Sanacorp	Excipial® U10 Lipolotio	321879	1
Galderma/Sanacorp	Excipial® U10 Lipolotio	323868	1

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Supplier	Substance	Batch	Spectra
Galderma/Sanacorp	Excipial® U10 Lipolotio	322729	1
Galderma/Würmtal-Apo.	Excipial® U10 Lipolotio	T053	1
Galderma/Würmtal-Apotheke	Excipial® U10 Lipolotio	V042	1
Spirig/AHD	Excipial® U10 Lipolotio	M025	1
Artesan	Fabitop® base cream	GLWW5	1
Artesan	Fabitop® base cream	GLWD4	1
Caelo	Fabitop® base cream	glwd2	1
Caelo	Fabitop® base cream	GWWL3	1
Fontapharm	Fabitop® base cream	GLWW4	1
Fontapharm	Fabitop® base cream	GLWD2	3
Fontapharm	Fabitop® base cream	GLWD2x2	1
Fontapharm	Fabitop® base cream	GLWD3	2
Fontapharm	Fabitop® base cream	101601	1
fontapharm AG	Fabitop® base cream	101601	1
Fontapharm/Gehe	Fabitop® base cream	GLWD4	1
Fontapharm/Noweda	Fabitop® base cream	GLWD3	1
Fontapharm/Noweda	Fabitop® base cream	101601	1
Fontapharm/Phönix	Fabitop® base cream	101601	7
Fontapharm/Sanacop	Fabitop® base cream	101601	3
Spangropharm	Fabitop® base cream	1016022	1
Fontapharma	Fabitop® base cream	GLWD2	6
Fontapharma AG / Noweda	Fabitop® base cream	1016021	1
Gehe	Fabitop® base cream	GRWW2	6
Jenne	Fabitop® base cream	GWWL1	1
jenne artesan	Fabitop® base cream	GLWWW5	1
Caelo	Fabitop® base cream	GWWL1	1
Phoenix/Artesan	Fabitop® base cream	GLWD5	3
Phönix	Fabitop® base cream	GLWD3	1
Phönix Fontapharm	Fabitop® base cream	101601	1
Phönix/Fontapharm	Fabitop® base cream	GRWW2	1
THC/Noweda	Fabitop® base cream	1016022	1
Caelo	Hans Karrer Lipocream MicroS...	LOT17001	1
Hans Karrer / Anzag	Hans Karrer Lipolotion Micro...	16004	1
Hans Karrer GmbH/Krieger	Hans Karrer Lipolotion Micro...	LOT19009	1
Hans Karrer/Gehe	Hans Karrer Lipolotion Micro...	17002	20
HansKarrer/Phönix	Hans Karrer Lipolotion Micro...	19004	1
KARRER/ E	Hans Karrer Lipolotion Micro...	LOT17002	1
Galderma	Lipoderm® lotion	R044	2
Galderma	Lipoderm® lotion	S021	1
Galderma	Lipoderm® lotion	T011	1
Galderma	Lipoderm® lotion	169310	1
Galderma/Alliance	Lipoderm® lotion	LOTV012	2
Galderma/Alliance	Lipoderm® lotion	50316	2
Galderma/AllianceHC	Lipoderm® lotion	T011	2
Galderma/Kehr	Lipoderm® lotion	S021	2
Galderma/Phoenix	Lipoderm® lotion	S041	1
Galderma/Phönix	Lipoderm® lotion	T043	1
Hedinger/Noweda	Lipoderm® lotion	169310	1
Ichthyol/Phönix	Lipoderm® lotion	LOTT043	1
Jenne	Lipoderm® lotion	T011	1
Nestle Skin Health	Lipoderm® lotion	169310	1
Noweda	Lipoderm® lotion	169310	1
spirig	Lipoderm® lotion	4622	1
Spirig	Lipoderm® lotion	R011	2
Spirig	Lipoderm® lotion	LOTR011	1
Spirig	Lipoderm® lotion	R023	2
Spirig	Lipoderm® lotion	S041	2
Spirig Pharma	Lipoderm® lotion	V012	1
Spirig Pharma AG	Lipoderm® lotion	N041	1
Spirig Pharma AG/Allian...	Lipoderm® lotion	NO41	1

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Supplier	Substance	Batch	Spectra
Spirig Pharma AG/Allian...	Lipoderm® lotion	N041	1
Spirig Pharma AG/Allian...	Lipoderm® lotion	R011	4
Spirig Pharma AG/Allian...	Lipoderm® lotion	R023	8
Spirig Pharma AG/Allian...	Lipoderm® lotion	R044	3
Spirig Pharma/Phoenix	Lipoderm® lotion	T043	2
Spirig/AHD	Lipoderm® lotion	N041	1
Spirig/AHD	Lipoderm® lotion	LOTN041	1
Spirig/AllianceHC	Lipoderm® lotion	S021	3
Spirig/Gehe	Lipoderm® lotion	S041	1
Spirig/Phoenix	Lipoderm® lotion	M065	4
SpirigPharm/Noweda	Lipoderm® lotion	LOT50932	1
AHD	Neribas® cream	YY02804	1
AHD	Neribas® cream	YY02H20	1
AHD	Neribas® cream	YY02TTH	1
AHD	Neribas® cream	YY0431K	1
AHD	Neribas® cream	YY02L84	1
AHD	Neribas® cream	YY0431J	1
Bayer/ Sanacorp	Neribas® cream	YY002L6	1
Caelo	Neribas® cream	yyo18ff	1
Caelo	Neribas® cream	YY01X64	1
Caelo	Neribas® cream	YY0203H	1
Caelo	Neribas® cream	yy01kk7	1
Chiesi / Gehe	Neribas® cream	32097A	1
Caelo	Neribas® cream	yy01k94	1
Caelo	Neribas® cream	yy0203H	1
GP GmbH/Spangro	Neribas® cream	Y018FF	1
GPGrenzach Produktion/P...	Neribas® cream	YY01673	1
Intendis / Gehe	Neribas® cream	21076A	1
Intendis / Sanacorp	Neribas® cream	24105A	1
Intendis GmbH	Neribas® cream	24089A	1
Jenapharm	Neribas® cream	33100C	1
Jenapharm	Neribas® cream	YY0203H	1
Jenapharm	Neribas® cream	YY02805	2
Jenapharm	Neribas® cream	YY0277H	1
Jenapharm / Gehe	Neribas® cream	34104C	1
Jenapharm / Gehe	Neribas® cream	YY02L84	1
Jenapharm / Noweda	Neribas® cream	YY02H20	2
Jenapharm / Sanacorp	Neribas® cream	YY02804	1
Jenapharm /Noweda	Neribas® cream	YY00C34	1
Jenapharm/	Neribas® cream	YY01KK7	1
Jenapharm/ G	Neribas® cream	YY01KK7	1
Jenapharm/ Noweda	Neribas® cream	YY00216	1
Jenapharm/ Noweda	Neribas® cream	YY01TCN	1
Jenapharm/Alliance	Neribas® cream	YY001HS	1
Jenapharm/Alliance	Neribas® cream	YY000C3	2
Jenapharm/Alliance	Neribas® cream	YY006LX	1
Jenapharm/gehe	Neribas® cream	yy02805	1
Jenapharm/Gehe	Neribas® cream	YY005HT	1
Jenapharm/Gehe	Neribas® cream	YY006KY	1
Jenapharm/Gehe	Neribas® cream	YY01KK7	1
Jenapharm/Noweda	Neribas® cream	YY00C35	2
Jenapharm/Noweda	Neribas® cream	YY00XEF	2
Jenapharm/Noweda	Neribas® cream	YY014NJ	2
Jenapharm/Noweda	Neribas® cream	YY01CXP	2
Jenapharm/Phönx	Neribas® cream	YY02H20	1
Karo Pharma	Neribas® cream	YY04EYL	1
Krieger	Neribas® cream	3388	1
Caelo	Neribas® cream	yy02805	1
Noweda/Jenapharm	Neribas® cream	YY00PF1	1
Noweda/Leopharm	Neribas® cream	YY02H20	1

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Supplier	Substance	Batch	Spectra
Phoenix	Neribas® cream	3094	1
Phoenix	Neribas® cream	3229	1
Phoenix	Neribas® cream	3378	1
Phönix	Neribas® cream	3139	1
Phönix / Jenapharm	Neribas® cream	YY01FX3	1
Römer/apo	Neribas® cream	YY005HT	2
Caelo	Neuroderm® moisturising cream	6051801	1
Infectopharm/Gehe	Neuroderm® moisturising cream	S0315081	1
Allergika Pharma GmbH	Allergika® Base cream		1
Chiesi	Asche Basis® cream	24220A	2
Chiesi GmbH/Gehe	Asche Basis® cream		2
Chiesi,Fa.Gehe	Asche Basis® cream		1
Chiesi,Gehe	Asche Basis® cream		1
Chiesi/Krieger	Asche Basis® cream		1
Dr.Wolff	Asche Basis® cream		1
Chiesi	Asche Basis® lotion	24049A	1
Chiesi	Asche Basis® lotion	64082A	1
KoKo GmbH/KoKo Gmbh	DMS® base cream classic		1
Beiersdorf	Eucerinum O/W basis	41830108WA	3
Beiersdorf	Eucerinum O/W basis	53430208WA	3
Beiersdorf	Eucerinum W/O basis	31230108WA	1
Beiersdorf	Eucerinum W/O basis	83730208WA	5
Spirig Pharma/Gehe	Excipial® hydro cream		1
Spirig/Gehe	Excipial® hydro cream		3
Alliance Healthcare	Excipial® lipo cream		2
spirig	Excipial® lipo cream		1
Fontapharm	Fabitop® base cream	GLWD5	1
	Neribas® cream	YY02H20	1
Caelo	Neuroderm® moisturising cream		3
Gehe	Neuroderm® moisturising cream		1
Infecto/Phönix	Neuroderm® moisturising cream		2
infectopharm	Neuroderm® moisturising cream		1
Infectopharm	Neuroderm® moisturising cream		6
InfectoPharm	Neuroderm® moisturising cream		17
Infectopharm/Alliance	Neuroderm® moisturising cream		4
Infectopharm/Fiebig	Neuroderm® moisturising cream		1
Infectopharm/Kehr	Neuroderm® moisturising cream		1
Infectopharm/noweda	Neuroderm® moisturising cream		1
Infectopharm/Noweda	Neuroderm® moisturising cream		3
Infectopharm/Phönix	Neuroderm® moisturising cream		8
InfectoPharma/Alliance ...	Neuroderm® moisturising cream		2
Infetopharm	Neuroderm® moisturising cream		1
Noweda	Neuroderm® moisturising cream		1
Bombastus	Neuroderm® moisturising cream		1
PHÖNIX	Neuroderm® moisturising cream		1
Sanacorp	Neuroderm® moisturising cream		1

- 6225 spectra from 705 *Apo-Ident* customers from a total of 2601 batches from a further 127 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Hydrophilic ointments* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose,

all relevant spectra of the various substances were compared with *Hydrophilic ointments* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type (*A*/*B*/*C*).

	False positive	True positive	False negative	True negative
Type A	0	3510	0	20 995
Type B	0	2107	113	17 891
Type C	0	2213	162	6199

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.8291 %)
Type B	100.0000 % (> 99.9440 %)	94.9099 % (> 94.7748 %)
Type C	100.0000 % (> 98.7894 %)	93.1789 % (> 93.0526 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Lipolotio urea 5% F body lotion	11.36	–
Dimeticone ointment 10% SR	12.82	–
Optiderm® lotion	15.14	–
Dexeryl®	15.51	–
Neuroderm® moisturising cream lipo	15.68	–
La Roche-Posay Toleriane	18.73	–
Allergika evening primrose oil cream 20%	24.99	–
Amciderm® Base cream	28.01	–
Linola® Sept	33.73	–
Dermifant® kids cream	35.18	–
Dermatop® base ointment	35.70	–
Nourivan™ Antiox	40.98	–
Linola® H fat N	60.15	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31869	31869	0.00	15.14
30845	30845	0.00	16.02
32916	32916	0.00	41.68
33968	33968	0.00	41.34
31072	31072	0.00	39.43
31535	31535	0.00	35.31
30828	30828	0.00	21.06
31068	31068	0.00	26.97
33737	33737	0.00	24.05
30713	30713	0.00	45.10
30993	30993	0.00	43.34
32767	32767	0.00	41.20
30775	30775	0.00	54.40
34044	34044	0.00	21.43
34359	34359	0.00	40.04
31085	31085	0.00	54.51
30732	30732	0.00	40.19
31280	31280	0.00	45.17
33194	33194	0.00	32.59
31070	31070	0.00	18.96
31058	31058	0.00	41.83
31539	31539	0.00	21.35
33195	33195	0.00	33.89
31772	31772	0.00	19.62
33213	33213	0.00	26.07
31061	31061	0.00	42.50
34117	34117	0.00	33.11
30725	30725	0.00	49.80
31115	31115	0.00	34.65
32997	32997	0.00	40.67
33969	33969	0.00	41.53
31578	31578	0.00	31.57
30722	30722	0.00	35.59
31102	31102	0.00	44.25
31761	31761	0.00	41.96
30726	30726	0.00	35.98
31511	31511	0.00	49.09
31874	31874	0.00	50.24
34043	34043	0.00	48.70
31730	31730	0.00	26.62
31095	31095	0.00	45.07
34119	34119	0.00	23.47
33668	33668	0.00	44.55
33669	33669	0.00	42.89
31873	31873	0.00	26.08
30634	30634	0.00	38.62

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31050	31050	0.00	43.04
30733	30733	0.00	33.01
31066	31066	0.00	30.21
31067	31067	0.00	39.30
31089	31089	0.00	45.75
31281	31281	0.00	29.64
31041	31041	0.00	19.98
33270	33270	0.00	40.48
33208	33208	0.00	44.55
32178	32178	0.00	42.20
31082	31082	0.00	59.41
33221	33221	0.00	40.40
33793	33793	0.00	16.37
31627	31627	0.00	18.89
34360	34360	0.00	16.28
31950	31950	0.00	19.43
31088	31088	0.00	47.12
33039	33039	0.00	19.39
31520	31520	0.00	49.49
35149	35149	0.00	13.53
33207	33207	0.00	45.79
33636	33636	0.00	44.97
31307	31307	0.00	15.36
31234	31234	0.00	33.89
32177	32177	0.00	32.53
31236	31236	0.00	36.67
31309	31309	0.00	47.07
31576	31576	0.00	59.08
31308	31308	0.00	45.82
31870	31870	0.00	43.32
30635	30635	0.00	35.96

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 2.3-2021-01

Validated substance/substance group	**Immortelle oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30450-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Immortelle oil; Oleum helichrysum italicum

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Immortelle oil	4	2	4

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Immortelle oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Immortelle oil	00324A27	34383	40	not required
Taoasis	Immortelle oil	L24113D-113148BAG90451	31138	40	not required
Taoasis	Immortelle oil	L24415DN-122092BAG90451	32069	60	not required
Taoasis	Immortelle oil	114717DNJ-137	33727	40	not required

Validation samples

A total of 53 906 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 *Immortelle oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Immortelle oil*.
- 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
Taoasis	Immortelle oil	L17716DN-126770	32975	40
Taoasis	Immortelle oil	L17716DN-124955	33021	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 4 batches from the substance/substance group *Immortelle oil*.

- 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
Taoasis	Immortelle oil	L03111DN	1
Taoasis	Immortelle oil	L38914DN-118878	2
Taoasis	Immortelle oil	L14717DNJ-132	1
Taoasis	Immortelle oil	L14717DNJ-3017	1

- 8595 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Immortelle oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Immortelle oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	5	0	8595

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7978 %)	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 *Immortelle oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Melissa oil	15.20	–
Ginger oil	15.79	–
Vetiver bourbon oil	21.72	–
Lemon grass oil	24.70	–
Citus oil	29.96	–
Myrtle oil	30.86	–
Cedar wood oil	33.64	–
Chamomile (essential oil)	34.54	–
Spearmint oil	40.44	–
Swiss pine oil	41.12	–
Patchouli oil	45.09	–
Marjoram oil	46.23	–
Cypress oil	46.50	–
Carrot seed oil	47.35	–
Hyssop oil	49.53	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31138	31138	0.00	25.37
32069	32069	0.00	20.46
33727	33727	0.00	29.40
34383	34383	0.00	27.82

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 2.3-2021-01

Validated substance/substance group	**Juniper oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31559-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Juniper oil; Oleum juniperi e baccarae

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Juniper oil	3	3	2

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Juniper oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Juniper oil	4155-116757	31559	60	not required
Taoasis	Juniper oil	4155-120900	31687	60	not required
Taoasis	Juniper oil	02JB0B-126047	32809	40	not required

Validation samples

A total of 53 906 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 *Juniper oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Juniper oil*.
- 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
Primavera	Juniper oil	00497L26	34398	40
Taoasis	Juniper oil	02JB0B-127283	32932	40
Taoasis	Juniper oil	1713-128196	33651	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Juniper oil*.

- 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	Juniper oil	16160706	1
Taoasis	Juniper oil	155-118896	1

- 8598 spectra from 736 *Apo-Ident* customers from a total of 3544 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Juniper oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Juniper oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	77	43	20 681
Type C	0	2	0	8598

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9455 %)	64.1667 % (> 61.6667 %)
Type C	100.0000 % (> 98.8173 %)	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 *Juniper oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dwarf pine oil	21.46	–
Spearmint oil	23.10	–
Frankincense oil	25.75	–
Spruce needle oil	28.34	–
Angelica root oil	29.52	–
Swiss pine oil	35.40	–
Pine silvestris oil	36.65	–
Silver fir oil	43.47	–
Citus oil	45.19	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32809	32809	0.00	21.92
31559	31559	0.00	24.24
31687	31687	0.00	25.88

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 2.3-2021-01

Validated substance/substance group	**La Roche-Posay Cold Cream Naturel**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30829-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

La Roche-Posay Cold Cream Naturel

Special notes

When selecting the *La Roche-Posay Cold Cream Naturel* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
La Roche-Posay Cold Cream Naturel	3	2	4

Second-stage model

For differentiation of the substance/substance group *La Roche-Posay Cold Cream Naturel* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *La Roche-Posay Cold Cream Naturel*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
La Roche-Posay	La Roche-Posay C…	54J01P	30829	40	not required
La Roche-Posay	La Roche-Posay C…	54K31P	31074	40	not required
La Roche-Posay	La Roche-Posay C…	54LN1P	31765	60	not required

Validation samples

A total of 53 906 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 *La Roche-Posay Cold Cream Naturel*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *La Roche-Posay Cold Cream Naturel*.
- 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
La Roche-Posay	La Roche-Posay Cold Cream Na…	54M51P	33262	40
La Roche-Posay	La Roche-Posay Cold Cream Na…	54P61P	33984	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 4 batches from the substance/substance group *La Roche-Posay Cold Cream Naturel*.
- 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
Gehe	La Roche-Posay Cold Cream Na…	54M91P	1
La Roche-Posay	La Roche-Posay Cold Cream Na…	54M91P	1
La Roche-Posay	La Roche-Posay Cold Cream Na…	54M01P	1
La Roche-Posay	La Roche-Posay Cold Cream Na…	54M11P	1
Mea-SanacorpWE10.02.201…	La Roche-Posay Cold Cream Na…	LOT54M91P	1

- 8595 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *La Roche-Posay Cold Cream Naturel* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *La Roche-Posay Cold Cream Naturel* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	5	0	8595

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7978 %)	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 *La Roche-Posay Cold Cream Naturel* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Stomahesive® adhesive paste	50.71	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30829	30829	0.00	80.28
31074	31074	0.00	83.77
31765	31765	0.00	83.07

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 2.3-2021-01

Validated substance/substance group	**La Roche-Posay Toleriane**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30827-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

La Roche-Posay Toleriane

Special notes

When selecting the *La Roche-Posay Toleriane* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
La Roche-Posay Toleriane	3	2	4

Second-stage model

For differentiation of the substance/substance group *La Roche-Posay Toleriane* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *La Roche-Posay Toleriane*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
La Roche-Posay	La Roche-Posay T…	54J901	30827	40	not required
La Roche-Posay	La Roche-Posay T…	54K500	31094	40	not required
La Roche-Posay	La Roche-Posay T…	54N201	32563	40	not required

Validation samples

A total of 53 906 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 *La Roche-Posay Toleriane*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 385 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *La Roche-Posay Toleriane*.
- 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
La Roche-Posay	La Roche-Posay Toleriane	54N600	32759	40
La Roche-Posay	La Roche-Posay Toleriane	54P401	33983	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 4 batches from the substance/substance group *La Roche-Posay Toleriane*.
- 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	La Roche-Posay Toleriane	54J500	1
Gehe	La Roche-Posay Toleriane	54P802	4
Roche Posay/Gehe	La Roche-Posay Toleriane	54R1011	1
Roche/AHD	La Roche-Posay Toleriane	54J800	1

- 8593 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *La Roche-Posay Toleriane* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *La Roche-Posay Toleriane* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	80	0	20 721
Type C	0	7	0	8593

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7941 %)	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 *La Roche-Posay Toleriane* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Eucerinum W/O basis	17.44	–
Neuroderm® moisturising cream	21.36	–
Excipial® U10 Lipolotio	22.61	–
DMS® base cream high classic	24.11	–
Base cream Taoasis	27.41	–
DMS® base cream classic	27.50	–
Hans Karrer Lipocream MicroSilver	27.73	–
Abitima® clinic body cream	28.88	–
Asche Basis® lotion	29.16	–
Excipial® U Lipolotio	29.60	–
Lipoderm® lotion	30.82	–
Dimeticone ointment 10% SR	34.85	–
Asche Basis® cream	35.31	–
Neribas® cream	39.83	–
Hans Karrer Lipolotion MicroSilver	41.85	–
Neuroderm® care lotion	42.34	–
Linola® body milk	42.37	–
DMS® base cream high classic plus	42.85	–
Excipial® hydro cream	50.85	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30827	30827	0.00	31.11
31094	31094	0.00	25.22
32563	32563	0.00	30.31

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 2.3-2021-01

Validated substance/substance group	**Lemon grass oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30661-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lemon grass oil; Cymbopoginis aetheroleum

Special notes

When selecting the *Lemon grass oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lemon grass oil	4	3	17

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Lemon grass oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bombastus	Lemon grass oil	263571	30661	40	not required
Bombastus	Lemon grass oil	278923	31185	40	not required
Bombastus	Lemon grass oil	278526	31187	40	not required
Taoasis	Lemon grass oil	130930-116754	31549	60	not required

Validation samples

A total of 53 906 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 *Lemon grass oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Lemon grass oil*.
- 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
Bombastus	Lemon grass oil	294338	33012	40
Primavera	Lemon grass oil	00536M26	34370	40
Taoasis	Lemon grass oil	1448-127048	32977	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 17 batches from the substance/substance group *Lemon grass oil*.

- 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
Bombastus	Lemon grass oil	270423	1
Bombastus	Lemon grass oil	308065	1
Caelo	Lemon grass oil	17004202	1
Primavera	Lemon grass oil	11401144	1
Primavera/Sanacorp	Lemon grass oil	484A25	1
Taoasis	Lemon grass oil	532897-111140	1
Taoasis	Lemon grass oil	13131-112982	1
Taoasis	Lemon grass oil	8911011-121890	1
Taoasis	Lemon grass oil	FFL457-123568	1
Taoasis	Lemon grass oil	1663-125423	1
Taoasis	Lemon grass oil	130930-115336	1
Taoasis	Lemon grass oil	18988-125876	1
Taoasis	Lemon grass oil	1448-126624	1
Taoasis	Lemon grass oil	1448-128742	1
Taoasis	Lemon grass oil	17004202	1
Taoasis	Lemon grass oil	1777-2776	1
Taoasis	Lemon grass oil	1448-507	1
Taoasis	Lemon grass oil	6093-6119	1

- 8582 spectra from 736 *Apo-Ident* customers from a total of 3529 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lemon grass oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lemon grass oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	119	1	20 681
Type C	0	18	0	8582

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9455 %)	99.1667 % (> 96.6667 %)
Type C	100.0000 % (> 98.7884 %)	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 *Lemon grass oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Patchouli oil	29.78	–
Carrot seed oil	30.39	–
Cypress oil	32.80	–
Immortelle oil	33.90	–
Marjoram oil	35.37	–
Tea tree oil	40.47	–
Myrtle oil	40.66	–
Ginger oil	41.38	–
Melissa oil	45.64	–
Vetiver bourbon oil	48.71	–
Citus oil	53.16	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31185	31185	0.00	32.28
31549	31549	0.00	37.60
30661	30661	0.00	39.68
31187	31187	0.00	29.78

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 2.3-2021-01

Validated substance/substance group	**Liniment ointments**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30731-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Liniment ointments; Amciderm® Base cream; Excipial® U Hydrolotio; Linola® O/W cream; Linola® Sept; Nourivan™ Antiox

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Amciderm® Base cream	2	2	5
Excipial® U Hydrolotio	4	2	25
Linola® O/W cream	3	0	0
Linola® Sept	3	1	0
Nourivan™ Antiox	3	0	1

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Liniment ointments*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Almirall	Amciderm® Base c...	313311	31509	60	not required
Almirall	Amciderm® Base c...	313311	31628	75	not required
Almirall	Amciderm® Base c...	650341	33502	40	not required
Spirig Pharma	Excipial® U Hydr...	M016	30731	40	not required
Spirig Pharma	Excipial® U Hydr...	M063	31073	40	not required
Spirig Pharma	Excipial® U Hydr...	N013	31279	40	not required
Spirig Pharma	Excipial® U Hydr...	R014	31536	60	not required
Dr. Wolff	Linola® O/W cream	238482	30834	40	not required
Dr. Wolff	Linola® O/W cream	334010	31133	40	not required
Dr. Wolff	Linola® O/W cream	432480	31312	40	not required
Dr. Wolff	Linola® Sept	334080	31079	40	not required
Dr. Wolff	Linola® Sept	509361	31856	60	not required
Dr. Wolff	Linola® Sept	707990	34126	40	not required
Fagron	Nourivan™ Antiox	14C11-T09-010959	31495	60	not required
Fagron	Nourivan™ Antiox	1503258	31958	45	not required
Fagron	Nourivan™ Antiox	1703842	33789	30	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 750 spectra of 16 reference samples from the substance/substance group *Liniment ointments*. These samples are listed above in the *calibration samples* section. The reference samples come from 15 different batches.
- 23 755 spectra from a total of 490 batches from further 156 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

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

- 345 spectra of 10 reference samples from the substance/substance group *Liniment ointments*.
- 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
Almirall	Amciderm® Base cream	538331	32758	40
Almirall	Amciderm® Base cream	822351	34365	40
Spirig Pharma	Excipial® U Hydrolotio	S061	33206	40
Spirig Pharma	Excipial® U Hydrolotio	V052	33981	40
Dr. Wolff	Linola® Sept	603190	32760	40
Dr. Wolff	Linola® Sept	603190	33257	40
Fagron	Nourivan™ Antiox	1503258	31958†	15
Fagron	Nourivan™ Antiox	1503258	32778	40
Fagron	Nourivan™ Antiox	1503258	32822	40
Fagron	Nourivan™ Antiox	1703842	33789†	10

- 20 456 spectra from a total of 440 batches from further 200 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 186 spectra from 66 *Apo-Ident* customers from 107 batches from the substance/substance group *Liniment ointments*.
- Among them are spectra of independent samples from 100 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Allmiral/Gehe	Amciderm® Base cream	418321	1
Almirall/Alliance	Amciderm® Base cream	650341	1
Almirall/Phönix	Amciderm® Base cream	538331	3
Almirall/Phönix	Amciderm® Base cream	822351	2
Almirall/Phönix	Amciderm® Base cream	12161	1
Fagron	Amciderm® Base cream	23102017	1
Caelo	Excipial® U Hydrolotio	LOTR092	1
Galderma	Excipial® U Hydrolotio	LOTR054	1
Galderma	Excipial® U Hydrolotio	T011	1
Galderma	Excipial® U Hydrolotio	V042	1
Galderma	Excipial® U Hydrolotio	172481	1
Galderma	Excipial® U Hydrolotio	302972	1
Galderma	Excipial® U Hydrolotio	50857	1
Galderma	Excipial® U Hydrolotio	306123	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
Galderma	Excipial® U Hydrolotio	1107483	1
Galderma	Excipial® U Hydrolotio	318203	1
Galderma/ Fiebig	Excipial® U Hydrolotio	LOTV022	1
Galderma/ Gehe	Excipial® U Hydrolotio	LOTR053	1
Galderma/Alliance	Excipial® U Hydrolotio	T072	2
Galderma/Alliance	Excipial® U Hydrolotio	50723	1
Galderma/Gehe	Excipial® U Hydrolotio	S014	1
Galderma/Gehe	Excipial® U Hydrolotio	50723	1
Galderma/Noweda	Excipial® U Hydrolotio	R054	1
Galderma/P	Excipial® U Hydrolotio	V051	1
Galderma/Phönix	Excipial® U Hydrolotio	T013	1
Galderma/Phönix	Excipial® U Hydrolotio	V011	1
Noweda	Excipial® U Hydrolotio	S061	1
Phoenix/Spirig	Excipial® U Hydrolotio	M016	1
PHÖNIX	Excipial® U Hydrolotio	V051	1
PHÖNIX	Excipial® U Hydrolotio	50593	1
SANACORP	Excipial® U Hydrolotio	172141	1
Spirig	Excipial® U Hydrolotio	N013	1
Spirig	Excipial® U Hydrolotio	NO13	1
Spirig Pharma	Excipial® U Hydrolotio	NO33	1
Spirig Pharma AG/ NOWEDA	Excipial® U Hydrolotio	LOTN022	1
Spirig Pharma AG/Noweda	Excipial® U Hydrolotio	R054	1
Spirig/Gehe	Excipial® U Hydrolotio	R054	3
AHD	Linola® O/W cream	437110	1
Caelo	Linola® O/W cream	lllllllll	1
Caelo	Linola® O/W cream	905070	1
Caelo	Linola® O/W cream	239181	1
Caelo	Linola® O/W cream	238520	2
Caelo	Linola® O/W cream	238484	1
Caelo	Linola® O/W cream	330760	1
Caelo	Linola® O/W cream	606100	1
Caelo	Linola® O/W cream	438350	1
Caelo	Linola® O/W cream	236281	1
Caelo	Linola® O/W cream	238530	2
chiesi / Noweda	Linola® O/W cream	331460	1
Dr Wolff/ Sanacorp	Linola® O/W cream	808420	1
Dr Wolff/ Sanacorp	Linola® O/W cream	810150	2
Dr. August Wolff GmbH &...	Linola® O/W cream	904680	1
Dr. August Wolff GmbH &...	Linola® O/W cream	903600	1
Dr. August Wolff GmbH &...	Linola® O/W cream	908380	1
Dr. August Wolff GmbH &...	Linola® O/W cream	170522LC/701090	1
Dr. August Wolff GmbH&C...	Linola® O/W cream	808420	1
Dr. August Wolff GmbH&C...	Linola® O/W cream	901150	2
Dr. August Wolff GmbH&C...	Linola® O/W cream	908930	1
Dr. August Wolff GmbH&C...	Linola® O/W cream	904890	2
Dr. August Wolff GmbH&C...	Linola® O/W cream	1750	1
Dr. August Wolff/ Jenne	Linola® O/W cream	1090	1
Dr. Wolf/GEHE	Linola® O/W cream	437110	1
Dr. Wolff	Linola® O/W cream	238520	2
Dr. Wolff	Linola® O/W cream	236290	1
Dr. Wolff	Linola® O/W cream	233200	1
Dr. Wolff	Linola® O/W cream	238484	1
Dr. Wolff	Linola® O/W cream	238530	2
Dr. Wolff	Linola® O/W cream	435080	1
Dr. Wolff	Linola® O/W cream	431200	3
Dr. Wolff	Linola® O/W cream	435530	1
Dr. Wolff	Linola® O/W cream	434430	3
Dr. Wolff	Linola® O/W cream	437120	1
Dr. Wolff	Linola® O/W cream	438200	2
Dr. Wolff	Linola® O/W cream	504100	1

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Supplier	Substance	Batch	Spectra
Dr. Wolff	Linola® O/W cream	508280	1
Dr. Wolff	Linola® O/W cream	505200	4
Dr. Wolff	Linola® O/W cream	512330	1
Dr. Wolff	Linola® O/W cream	602300	1
Dr. Wolff	Linola® O/W cream	510792	1
Dr. Wolff	Linola® O/W cream	510430	2
Dr. Wolff	Linola® O/W cream	602190	3
Dr. Wolff	Linola® O/W cream	605419	1
Dr. Wolff	Linola® O/W cream	606121	1
Dr. Wolff	Linola® O/W cream	605410	2
Dr. Wolff	Linola® O/W cream	901150	1
DR. WOLFF	Linola® O/W cream	234192	1
Dr. Wolff 25.03.2013 S...	Linola® O/W cream	236290	3
Dr. Wolff / Sanacorp	Linola® O/W cream	338990	3
Dr. Wolff / Sanacorp	Linola® O/W cream	905070	1
Dr. Wolff GmbH / Phoenix	Linola® O/W cream	606100	1
Dr. Wolff/ Jenne	Linola® O/W cream	904680	1
Dr. Wolff/ Noweda	Linola® O/W cream	901150	1
Dr. Wolff/Gehe	Linola® O/W cream	434320	2
Dr. Wolff/Gehe	Linola® O/W cream	138350	1
Dr. Wolff/Malteser	Linola® O/W cream	330751	1
Dr. Wolff/Malteser	Linola® O/W cream	333880	1
Dr. Wolff/Malteser	Linola® O/W cream	338990	1
Dr.August Wolff	Linola® O/W cream	233140	1
Dr.August Wolff	Linola® O/W cream	607140	1
Dr.August Wolff	Linola® O/W cream	605560	1
Dr.August Wolff	Linola® O/W cream	505560	1
Dr.August Wolff/Ebert	Linola® O/W cream	333640	2
Dr.August Wolff/Ebert	Linola® O/W cream	432970	1
Dr.August Wolff/Ebert	Linola® O/W cream	431250	1
Dr.Wolff	Linola® O/W cream	238482	1
Dr.Wolff	Linola® O/W cream	238530	1
Dr.Wolff	Linola® O/W cream	334003	1
Dr.Wolff	Linola® O/W cream	333640	1
Dr.Wolff	Linola® O/W cream	432490	1
Dr.Wolff	Linola® O/W cream	438200	1
Dr.Wolff	Linola® O/W cream	438360	1
Dr.Wolff	Linola® O/W cream	607140	1
Dr.Wolff	Linola® O/W cream	807360	1
Dr.Wolff	Linola® O/W cream	903600	1
Dr.Wolff / Phö	Linola® O/W cream	908930	1
Dr.Wolff / Phö	Linola® O/W cream	910420	2
Dr.Wolff/ Anzag	Linola® O/W cream	234193	1
Dr.Wolff/Anzag	Linola® O/W cream	238520	2
Dr.Wolff/Fiebig	Linola® O/W cream	606120	1
Dr.Wolff/Fiebig	Linola® O/W cream	510430	1
Dr.Wolff/Gehe	Linola® O/W cream	238520	1
Dr.Wolff/Gehe	Linola® O/W cream	432490	2
Dr.Wolff/Gehe	Linola® O/W cream	438360	1
Dr.Wolff/Gehe	Linola® O/W cream	606100	1
Dr.Wolff/Noweda	Linola® O/W cream	233200	1
Dr.Wolff/Phoenix	Linola® O/W cream	903600	1
Dr.Wolff/Phoenix	Linola® O/W cream	904680	1
Euro OTC	Linola® O/W cream	333730	1
Gehe	Linola® O/W cream	607140	1
Gehe/Dr Wolff	Linola® O/W cream	903600	1
Hedinger	Linola® O/W cream	908930	1
Infectopharm Sanacorp	Linola® O/W cream	810780	1
Phö/Dr.Wolff	Linola® O/W cream	901100	1
Phoenix/Wolff	Linola® O/W cream	333640	1

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Supplier	Substance	Batch	Spectra
wolff	Linola® O/W cream	434320	1
Wolff / Gehe	Linola® O/W cream	431130	3
Wolff / Noweda	Linola® O/W cream	431120	4
Wolff GmbH/Sanacorp	Linola® O/W cream	903540	1
Wolff/ Sanacorp	Linola® O/W cream	908930	1
Wolff/Sanacorp	Linola® O/W cream	333630	2
Fagron	Nourivan™ Antiox	150325	1
Dr. August Wolff GmbH &...	Linola® O/W cream		1
Dr. Wolff	Linola® O/W cream	432480	1
Fagron	Nourivan™ Antiox	1503258	3

- 8414 spectra from 736 *Apo-Ident* customers from a total of 3449 batches from a further 146 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	750	0	23 755
Type B	0	305	40	20 324
Type C	0	182	4	8413

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.2000 %)
Type B	100.0000 % (> 99.9449 %)	88.4058 % (> 87.5362 %)
Type C	100.0000 % (> 98.8052 %)	97.8495 % (> 96.2366 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Hans Karrer Hydrocream MicroSilver	10.83	–
Sebexol® basic pH 5 formula basis	11.35	–
Sebexol® cream lotion pH 5	15.92	–
Dimeticone ointment 10% SR	17.51	–
Wofacutan wash lotion	19.55	–
Abitima® clinic face cream	21.15	–
Base cream Taoasis	23.35	–
Optiderm® lotion	30.52	–
Hans Karrer Lipolotion MicroSilver	30.85	–
Neuroderm® moisturising cream	32.71	–
Asche Basis® lotion	35.72	–
Eucerinum W/O basis	38.70	–
Excipial® U10 Lipolotio	40.98	–
Fabitop® base cream	41.36	–
Fenistil® Gel	43.37	–
DMS® base cream classic	48.58	–
DMS® base cream high classic	51.29	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31133	31133	0.00	30.88
31509	31509	0.00	30.67
31856	31856	0.00	30.16
31628	31628	0.00	30.47
33502	33502	0.00	32.58
30834	30834	0.00	30.43
31495	31495	0.00	21.09
33789	33789	0.00	20.67
31079	31079	0.00	30.56
31958	31958	0.00	22.03
34126	34126	0.00	32.22
31312	31312	0.00	27.25
30731	30731	0.00	10.81
31073	31073	0.00	10.52
31279	31279	0.00	10.43
31536	31536	0.00	10.70

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 2.3-2021-01

Validated substance/substance group	**Linola® fat creme / Linola® H fat N / Alfason® Repair**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30724-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Linola® fat creme / Linola® H fat N / Alfason® Repair; Alfason® Repair; Linola® fat cream; Linola® H fat N

Special notes

When selecting the *Linola® fat creme / Linola® H fat N / Alfason® Repair* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Alfason® Repair	4	1	11
Linola® fat cream	4	3	38
Linola® H fat N	3	1	1

Second-stage model

For differentiation of the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Astellas Pharma	Alfason® Repair	12F18/77	30724	55	not required
Astellas Pharma	Alfason® Repair	13E16/76	31069	40	not required
Astellas Pharma	Alfason® Repair	16G60/75	32993	40	not required
LEO Pharma GmbH	Alfason® Repair	17E20/75	33790	40	not required
Dr. Wolff	Linola® fat cream	235260	30771	40	not required
Dr. Wolff	Linola® fat cream	337280	31096	40	not required
Dr. Wolff	Linola® fat cream	611011	33243	40	not required
Dr. Wolff	Linola® fat cream	612211	33260	40	not required
Dr. Wolff	Linola® H fat N	333080	31092	40	not required
Dr. Wolff	Linola® H fat N	611060	33211	40	not required
Dr. Wolff	Linola® H fat N	801410	34128	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 455 spectra of 11 reference samples from the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair*. These samples are listed above in the *calibration samples* section. The reference samples come from 11 different batches.

- 24 050 spectra from a total of 493 batches from further 158 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Linola® fat creme / Linola® H fat N / Alfason® Repair*.

- 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
Astellas Pharma	Alfason® Repair	15K07/77	32562	40
Dr. Wolff	Linola® fat cream	603820	32561	40
Dr. Wolff	Linola® fat cream	607250	34125	40
Dr. Wolff	Linola® fat cream	802990	34253	40
Dr. Wolff	Linola® H fat N	603230	32560	40
Dr. Wolff	Linola® H fat N	611060	33038	40

- 20 561 spectra from a total of 441 batches from further 201 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 64 spectra from 28 *Apo-Ident* customers from 50 batches from the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair*.

- Among them are spectra of independent samples from 50 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Astellas	Alfason® Repair	15J09/75	1
Astellas	Alfason® Repair	13H02/76	1
GEHE	Alfason® Repair	17K83/75	1
GEHE	Alfason® Repair	17J13/76	1
GEHE	Alfason® Repair	18EB5/75	1
GEHE	Alfason® Repair	17J11/79	1
GEHE	Alfason® Repair	18I90/75	1
Phoenix	Alfason® Repair	15/03/75	1
Phönix	Alfason® Repair	15J09/75	1
PHÖNIX	Alfason® Repair	17E81/75	2
PHÖNIX	Alfason® Repair	17E77/75	2
PHÖNIX	Alfason® Repair	17F72/75	1
Caelo	Linola® fat cream	435161	1
Caelo	Linola® fat cream	238540	1
Caelo	Linola® fat cream	438070	1
Caelo	Linola® fat cream	700320	1
Caelo	Linola® fat cream	803320	1
Dr. Wolff	Linola® fat cream	237920	1
Dr. Wolff	Linola® fat cream	333650	1
Dr. Wolff	Linola® fat cream	432591	1
Dr. Wolff	Linola® fat cream	437270	1
Dr. Wolff	Linola® fat cream	705555650	1
Dr. Wolff	Linola® fat cream	610320	1
Dr. Wolff	Linola® fat cream	810180	1
Dr. Wolff	Linola® fat cream	101808	1
Dr. Wolff	Linola® fat cream	907070	1
Dr. Wolff	Linola® fat cream	907080	2

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Supplier	Substance	Batch	Spectra
Dr. Wolff	Linola® fat cream	909790	1
Dr. Wolff / Alliance He...	Linola® fat cream	709800	1
Dr. Wolff / Gehe	Linola® fat cream	337860	1
Dr. Wolff /Anzag	Linola® fat cream	237710	1
Dr. Wolff 03.12.2013Fa....	Linola® fat cream	337701	1
Dr. Wolff/ Sanacorp	Linola® fat cream	3400	1
Dr. Wolff/Phönix	Linola® fat cream	700310	1
Dr. Wolff/Phönix	Linola® fat cream	810170	1
Dr. Wolff/Phönix	Linola® fat cream	909790	1
Dr.August Wolff Gmbh&Co...	Linola® fat cream	710080	1
Dr.August Wolff Gmbh&Co...	Linola® fat cream	810180	1
Dr.August Wolff Gmbh&Co...	Linola® fat cream	909790	1
dr.wolff	Linola® fat cream	337760	1
dr.wolff	Linola® fat cream	337770	1
Dr.Wolff	Linola® fat cream	608210	1
Dr.Wolff	Linola® fat cream	431160	1
Dr.Wolff	Linola® fat cream	701590	1
Dr.Wolff	Linola® fat cream	810170	1
Dr.Wolff - Noweda	Linola® fat cream	808280	1
Dr.Wolff/NOW	Linola® fat cream	435160	1
Dr.Wolff/Sanacorp	Linola® fat cream	704020	1
Dr.Wolff/Sanacorp	Linola® fat cream	700320	1
Löwen City-Apotheke Bar...	Linola® fat cream	231060	1
Phönix	Linola® fat cream	238540	1
Spangro 26.02.2014	Linola® fat cream	337760	1
Wolff	Linola® fat cream	608200	1
Wolff / Wolff	Linola® fat cream	431190	1
Wolff/Noweda	Linola® fat cream	704030	1
Wolff/Phöenix	Linola® fat cream	710060	1
Wolff/Phöenix	Linola® fat cream	807620	1
Wolff/Phönix	Linola® fat cream	710080	1
Wolff/Phönix	Linola® fat cream	907070	1
Wollf/Phönix	Linola® fat cream	337770	1
Engel-Apotheke	Linola® H fat N	2319Q-07101	1

- 8536 spectra from 736 *Apo-Ident* customers from a total of 3496 batches from a further 147 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	455	0	24 050
Type B	0	238	2	20 548
Type C	0	57	7	8536

The substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair* can be clearly distinguished from all other substances. In order to make these figures comparable, the

weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9600 %)	100.0000 % (> 98.6813 %)
Type B	100.0000 % (> 99.9457 %)	99.1667 % (> 97.9167 %)
Type C	100.0000 % (> 98.7858 %)	89.0625 % (> 84.3750 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Alfason Basis Cresa®	10.45	–
Dermatop® base ointment	14.72	–
Excipial® lipo cream	29.73	–
Lipolotio urea 5% F body lotion	54.75	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Linola® fat creme / Linola® H fat N / Alfason® Repair* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30771	30771	0.00	16.44
31096	31096	0.00	19.14
31092	31092	0.00	17.70
33211	33211	0.00	22.03
33790	33790	0.00	16.90
33243	33243	0.00	22.72
34128	34128	0.00	24.64
33260	33260	0.00	21.88
32993	32993	0.00	15.59

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30724	30724	0.00	20.23
31069	31069	0.00	9.00

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 2.3-2021-01

Validated substance/substance group	**Lipolotio urea 5% F body lotion**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30973-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lipolotio urea 5% F body lotion

Special notes

When selecting the *Lipolotio urea 5% F body lotion* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lipolotio urea 5% F body lotion	3	1	1

Second-stage model

For differentiation of the substance/substance group *Lipolotio urea 5% F body lotion* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Lipolotio urea 5% F body lotion*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Allergika	Lipolotio urea 5…	1205050	30973	80	not required
Allergika	Lipolotio urea 5…	13112021	31766	60	not required
Allergika	Lipolotio urea 5…	1801022	34362	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 180 spectra of 3 reference samples from the substance/substance group *Lipolotio urea 5% F body lotion*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.

- 24 325 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Lipolotio urea 5% F body lotion*.

- 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
Allergika	Lipolotio urea 5% F body lot…	1502011	32766	40
Allergika	Lipolotio urea 5% F body lot…	1502011	33482	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Lipolotio urea 5% F body lotion*.

- 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
Allergika/Ebert	Lipolotio urea 5% F body lot…	1810043	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lipolotio urea 5% F body lotion* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lipolotio urea 5% F body lotion* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	1	0	8599

The substance/substance group *Lipolotio urea 5% F body lotion* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8499 %)	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 *Lipolotio urea 5% F body lotion* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Neuroderm® moisturising cream lipo	16.10	–
Dermatest base ointment	16.65	–
Allergika evening primrose oil cream 20%	36.28	–
Excipial® U Lipolotio	37.25	–
Dermifant® kids cream	50.22	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lipolotio urea 5% F body lotion* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31766	31766	0.00	34.61
30973	30973	0.00	20.61
34362	34362	0.00	28.04

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 2.3-2021-01

Validated substance/substance group	**Lygal® head ointment N 3%**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31049-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lygal® head ointment N 3%

Special notes

When selecting the *Lygal® head ointment N 3%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lygal® head ointment N 3%	2	2	10

Second-stage model

For differentiation of the substance/substance group *Lygal® head ointment N 3%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Lygal® head ointment N 3%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taurus	Lygal® head oint…	124311	31049	40	not required
Taurus	Lygal® head oint…	143710	31763	60	not required

Validation samples

A total of 53 906 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 *Lygal® head ointment N 3%*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 405 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Lygal® head ointment N 3%*.
- 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
Taurus	Lygal® head ointment N 3%	160732	32763	40
Taurus	Lygal® head ointment N 3%	181802	34127	40
Taurus	Lygal® head ointment N 3%	160732	33261	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 5 *Apo-Ident* customers from 10 batches from the substance/substance group *Lygal® head ointment N 3%*.

- 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
Almirall	Lygal® head ointment N 3%	181908	1
Almirall	Lygal® head ointment N 3%	174928	1
Almirall/GEHE	Lygal® head ointment N 3%	174924	1
Almirall/GEHE	Lygal® head ointment N 3%	193815	1
Almirall/GEHE	Lygal® head ointment N 3%	184027	2
Almirall/GEHE	Lygal® head ointment N 3%	184028	1
Almirall/Otto	Lygal® head ointment N 3%	182913	1
Caelo	Lygal® head ointment N 3%	181909	1
Fagron	Lygal® head ointment N 3%	181905	1
Taurus Pharma	Lygal® head ointment N 3%	134507	1

- 8589 spectra from 736 *Apo-Ident* customers from a total of 3536 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lygal® head ointment N 3%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Lygal® head ointment N 3%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 405
Type B	0	120	0	20 681
Type C	0	11	0	8589

The substance/substance group *Lygal® head ointment N 3%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 94.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7907 %)	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 *Lygal® head ointment N 3%* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lygal® ointment base	38.92	–
Stomahesive® adhesive paste	55.39	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lygal® head ointment N 3%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31049	31049	0.00	38.92
31763	31763	0.00	39.06

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 2.3-2021-01

Validated substance/substance group	**Lygal® ointment base**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31014-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Lygal® ointment base

Special notes

When selecting the *Lygal® ointment base* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Lygal® ointment base	3	2	25

Second-stage model

For differentiation of the substance/substance group *Lygal® ointment 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 *Lygal® ointment base*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taurus	Lygal® ointment …	121302P	31014	40	not required
Taurus	Lygal® ointment …	154841	32749	40	not required
Taurus	Lygal® ointment …	164201	32772	40	not required
Taurus	Lygal® ointment …	164201	33244	40	not required
Taurus	Lygal® ointment …	164201	33297	40	not required

Validation samples

A total of 53 906 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 *Lygal® ointment base*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 305 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Lygal® ointment base*.
- 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
Almirall	Lygal® ointment base	174104	33988	40
Taurus	Lygal® ointment base	124904P	31704	60

- 20 701 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 59 spectra from 26 *Apo-Ident* customers from 26 batches from the substance/substance group *Lygal® ointment base*.

- 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
Almiral / Gehe	Lygal® ointment base	175007	4
Almiral / Gehe	Lygal® ointment base	175008	2
Almiral / Gehe	Lygal® ointment base	182905	2
Almiral/ Phönix	Lygal® ointment base	174106	1
Almirall	Lygal® ointment base	175007	2
Almirall	Lygal® ointment base	174106	2
Almirall	Lygal® ointment base	175008	1
Almirall	Lygal® ointment base	182002	1
Almirall	Lygal® ointment base	182904	2
Almirall	Lygal® ointment base	182001	1
ALmirall	Lygal® ointment base	182903	2
almirall Hermal GmbH	Lygal® ointment base	192701	1
almirall/gehe	Lygal® ointment base	174106	1
Almirall/GEHE	Lygal® ointment base	182903	1
Almirall/GE-HH	Lygal® ointment base	202503	1
Almirall/Noweda	Lygal® ointment base	175008	1
Almirall/Noweda	Lygal® ointment base	182903	1
Caelo	Lygal® ointment base	174106	1
Caelo	Lygal® ointment base	141601P	1
Caelo	Lygal® ointment base	154841	1
Caelo	Lygal® ointment base	182903	1
Finteler Apotheke	Lygal® ointment base	1704011	1
Phoenix WE: 08.11.17 20...	Lygal® ointment base	172803_2	1
Sanacorp/Almirall	Lygal® ointment base	175008	1
TAUROS PHARMA	Lygal® ointment base	124803	1
TAUROS PHARMA	Lygal® ointment base	141601P	1
Taurus	Lygal® ointment base	124803	2
Taurus	Lygal® ointment base	133401T	2
Taurus	Lygal® ointment base	141601T	1
Taurus	Lygal® ointment base	133402	1
Taurus	Lygal® ointment base	141603	2
Taurus	Lygal® ointment base	18121705	1
Taurus / Gehe	Lygal® ointment base	1704011	1
Taurus Pharma	Lygal® ointment base	133401P	1
Taurus Pharma	Lygal® ointment base	133401T	2
TAURUS PHARMA	Lygal® ointment base	141602T	1

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Supplier	Substance	Batch	Spectra
TAURUS PHARMA	Lygal® ointment base	154841	1
Taurus Pharma / Gehe	Lygal® ointment base	133401T	1
Taurus Pharma GmbH	Lygal® ointment base	164803	1
Taurus Pharma GmbH	Lygal® ointment base	172803_2	1
Taurus/ Phönix	Lygal® ointment base	133401T	1
Taurus/Alliance	Lygal® ointment base	1717022	2
Taurus/Alliance	Lygal® ointment base	1717021	1
Taurus/Phönix	Lygal® ointment base	154841	1
TAUROS PHARMA	Lygal® ointment base		1

- 8541 spectra from 735 *Apo-Ident* customers from a total of 3520 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Lygal® ointment 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 *Lygal® ointment 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	200	0	24 305
Type B	0	100	0	20 701
Type C	0	57	2	8541

The substance/substance group *Lygal® ointment 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 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 94.0000 %)
Type C	100.0000 % (> 98.7859 %)	96.6102 % (> 91.5254 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lygal® ointment base* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lygal® head ointment N 3%	20.13	–
Stomahesive® adhesive paste	38.62	–
Asche Basis® fat ointment	106.09	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lygal® ointment 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
32772	32772	0.00	31.49
33297	33297	0.00	23.68
33244	33244	0.00	27.92
31014	31014	0.00	21.76
32749	32749	0.00	26.05

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 2.3-2021-01

Validated substance/substance group	**Mandarin oil, green**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33798-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Mandarin oil, green

Special notes

When selecting the *Mandarin oil, green* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Mandarin oil, green	2	2	1

Second-stage model

For differentiation of the substance/substance group *Mandarin oil, green* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Mandarin oil, green*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Mandarin oil, gr…	00431E25	33798	40	not required
Primavera	Mandarin oil, gr…	00381H25	33806	40	not required

Validation samples

A total of 53 906 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 *Mandarin oil, green*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Mandarin oil, green*.
- 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
Primavera	Mandarin oil, green	00425M25	33960	40
Primavera	Mandarin oil, green	00350J26	34397	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Mandarin oil, green*.

- 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
Taoasis	Mandarin oil, green	110776-2806	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Mandarin oil, green* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Mandarin oil, green* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	80	0	20 721
Type C	0	1	0	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8499 %)	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 *Mandarin oil, green* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citric oil	25.36	–
Lime oil	29.31	–
Grapefruit oil, organic	36.64	–
Orange oil	50.16	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33798	33798	0.00	24.89
33806	33806	0.00	25.29

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 2.3-2021-01

Validated substance/substance group	**Manuka oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31545-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Manuka oil; Oleum leptospermum scoparium

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Manuka oil	4	2	10

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Manuka oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Manuka oil	1235-116650	31545	60	not required
Taoasis	Manuka oil	14286-119821	31655	60	not required
Taoasis	Manuka oil	83579-2408	33994	40	not required
Taoasis	Manuka oil	5181-9263	35075	40	not required

Validation samples

A total of 53 906 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 *Manuka oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Manuka oil*.
- 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
Primavera	Manuka oil	00476A27	34390	40
Taoasis	Manuka oil	42798-125299	32799	40
Taoasis	Manuka oil	42798-125299	33198	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 11 batches from the substance/substance group *Manuka oil*.

- 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
Taoasis	Manuka oil	36968-121509	1
Taoasis	Manuka oil	23694-123569	1
Taoasis	Manuka oil	42798-125299	3
Taoasis	Manuka oil	65261-127051	1
Taoasis	Manuka oil	42798-126332	2
Taoasis	Manuka oil	23694-122415	1
Taoasis	Manuka oil	83579-2220	4
Taoasis	Manuka oil	96134-2927	3
Taoasis	Manuka oil	2501-3536	1
Taoasis	Manuka oil	96134-2223	1
Canea Pharma GmbH	Manuka oil		1

- 8581 spectra from 736 *Apo-Ident* customers from a total of 3535 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Manuka oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Manuka oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	120	0	20 681
Type C	0	19	0	8581

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7882 %)	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 *Manuka oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Vetiver bourbon oil	12.98	–
Myrtle oil	35.68	–
Immortelle oil	37.72	–
Citus oil	40.10	–
Cardamom oil	47.38	–
Marjoram oil	47.58	–
Hyssop oil	48.06	–
Cumin oil	49.45	–
Cedar wood oil	54.40	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
35075	35075	0.00	22.29
31545	31545	0.00	34.53
31655	31655	0.00	33.78
33994	33994	0.00	25.40

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 2.3-2021-01

Validated substance/substance group	**Marjoram oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30454-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Marjoram oil; Majoranae aetheroleum

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Marjoram oil	5	1	20

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Marjoram oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Marjoram oil	16170005	32819	40	not required
Caelo	Marjoram oil	190992	34436	40	20190410*
Taoasis	Marjoram oil	130312-111991BAG90451	31137	40	not required
Taoasis	Marjoram oil	3701004-121123	32067	60	not required
Taoasis	Marjoram oil	1700187-3444	34275	40	not required

Validation samples

A total of 53 906 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 *Marjoram oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.
- 24 285 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Marjoram oil*.
- 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
Taoasis	Marjoram oil	1838-125624	32478	40
Caelo	Marjoram oil	16170005	32919	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 33 spectra from 9 *Apo-Ident* customers from 20 batches from the substance/substance group *Marjoram oil*.
- 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
Bombastus	Marjoram oil	278279	1
Caelo	Marjoram oil	13121301	1
Caelo	Marjoram oil	18028305	1
Caelo	Marjoram oil	12041602	7
Caelo	Marjoram oil	15051505	1
Caelo	Marjoram oil	13041603	2
Caelo	Marjoram oil	13041606	1
Caelo	Marjoram oil	14198304	1
Caelo	Marjoram oil	13041601	1
Taoasis	Marjoram oil	29293-98717	1
Taoasis	Marjoram oil	130312-111347	1
Taoasis	Marjoram oil	130312-111870	1
Taoasis	Marjoram oil	130910-116960	1
Taoasis	Marjoram oil	130910-117430	1
Taoasis	Marjoram oil	3701004-119994	2
Taoasis	Marjoram oil	1631-122347	1
Taoasis	Marjoram oil	1631-124621	1
Taoasis	Marjoram oil	1838-127470	3
Taoasis	Marjoram oil	1987-1387	3
Taoasis	Marjoram oil	1987-767	1
Taoasis/Gehe	Marjoram oil	29293-98717	1

- 8567 spectra from 736 *Apo-Ident* customers from a total of 3526 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Marjoram oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Marjoram oil* and it was evaluated

how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 285
Type B	0	80	0	20 721
Type C	0	32	1	8567

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7867 %)	96.9697 % (> 87.8788 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Carrot seed oil	22.75	–
Tea tree oil	26.42	–
Cypress oil	63.51	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32819	32819	0.00	52.46
34436	34436	0.00	45.25

continued on the next page

continued from previous page

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
34275	34275	0.00	68.11
31137	31137	0.00	66.48
32067	32067	0.00	41.60

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 2.3-2021-01

Validated substance/substance group	**Matricaria oil, morrocan**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30844-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Matricaria oil, morrocan; Oleum ormenis multicaulis

Special notes

When selecting the *Matricaria oil, morrocan* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Matricaria oil, morrocan	3	3	5

Second-stage model

For differentiation of the substance/substance group *Matricaria oil, morrocan* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Matricaria oil, morrocan*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Matricaria oil, ...	140124-116959	31579	60	not required
Taoasis	Matricaria oil, ...	6121017-122184	31841	60	not required
Taoasis	Matricaria oil, ...	1629-124596	32269	40	not required

Validation samples

A total of 53 906 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 *Matricaria oil, morrocan*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Matricaria oil, morrocan*.
- 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
Taoasis	Matricaria oil, morrocan	6982-1074109BAC90451	30844	40
Taoasis	Matricaria oil, morrocan	1629-125295	32480	40
Taoasis	Matricaria oil, morrocan	1814-126707	33020	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 5 batches from the substance/substance group *Matricaria oil, morrocan*.

- 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
Taoasis	Matricaria oil, morrocan	6159-93239	1
Taoasis	Matricaria oil, morrocan	6631-104465	1
Taoasis/Taoasis	Matricaria oil, morrocan	1814-127407	1
Taoasis/Taoasis	Matricaria oil, morrocan	5081-8452	1
Taoasis/Taoasis	Matricaria oil, morrocan	2022-960	1

- 8595 spectra from 736 *Apo-Ident* customers from a total of 3541 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Matricaria oil, morrocan* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Matricaria oil, morrocan* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	111	9	20 681
Type C	0	3	2	8595

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9455 %)	92.5000 % (> 90.0000 %)
Type C	100.0000 % (> 98.7978 %)	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 *Matricaria oil, morrocan* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Thyme oil, white	28.81	–
Citus oil	40.45	–
Marjoram oil	43.17	–
Angelica root oil	45.44	–
Carrot seed oil	52.85	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31579	31579	0.00	37.70
31841	31841	0.00	39.75
32269	32269	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 2.3-2021-01

Validated substance/substance group	**Matricaria oil, roman**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31254-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Matricaria oil, roman; Oleum anthemis nobilis

Special notes

When selecting the *Matricaria oil, roman* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Matricaria oil, roman	3	1	9

Second-stage model

For differentiation of the substance/substance group *Matricaria oil, roman* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Matricaria oil, roman*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Matricaria oil, …	34561-112874	31254	40	not required
Taoasis	Matricaria oil, …	1850119-119823	31686	60	not required
Taoasis	Matricaria oil, …	2033-843	33989	40	not required

Validation samples

A total of 53 906 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 *Matricaria oil, roman*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Matricaria oil, roman*.
- 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
Taoasis	Matricaria oil, roman	8941-125875	32796	40
Taoasis	Matricaria oil, roman	8941-125875	32978	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 9 batches from the substance/substance group *Matricaria oil, roman*.

- 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
Taoasis	Matricaria oil, roman	1850119-116753	1
Taoasis	Matricaria oil, roman	1850119-118138	1
Taoasis	Matricaria oil, roman	1850119-121467	1
Taoasis	Matricaria oil, roman	1850119-119451	1
Taoasis	Matricaria oil, roman	1511-122183	1
Taoasis	Matricaria oil, roman	8941-125875	1
Taoasis	Matricaria oil, roman	1638-123706	1
Taoasis	Matricaria oil, roman	1930-126600	7
Taoasis	Matricaria oil, roman	2033-3091	5

- 8581 spectra from 736 *Apo-Ident* customers from a total of 3537 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Matricaria oil, roman* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Matricaria oil, roman* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	70	10	20 721
Type C	0	19	0	8581

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	87.5000 % (> 83.7500 %)
Type C	100.0000 % (> 98.7882 %)	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 *Matricaria oil, roman* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hyssop oil	33.96	–
Sage oil	36.23	–
Rosemary camphor oil	49.91	–
Citus oil	54.57	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31254	31254	0.00	36.23
31686	31686	0.00	37.27
33989	33989	0.00	33.96

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 2.3-2021-01

Validated substance/substance group	**Melissa oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33800-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Melissa oil

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Melissa oil	4	1	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Melissa oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Melissa oil	00720H25	33800	40	not required
Primavera	Melissa oil	00010J26	34298	30	not required
Primavera	Melissa oil	00026A27	34404	40	not required
Taoasis	Melissa oil	640	33831	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 150 spectra of 4 reference samples from the substance/substance group *Melissa oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 355 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Melissa oil*.
- 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
Primavera	Melissa oil	00065E26	34166	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Melissa oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	150	0	24 355
Type B	0	0	40	20 761
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.0000 %)
Type B	100.0000 % (> 99.9460 %)	0.0000 % (≥ 0.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Melissa oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Immortelle oil	15.31	–
Ginger oil	23.06	–
Lemon grass oil	32.50	–
Cedar wood oil	33.30	–
Spearmint oil	35.58	–
Swiss pine oil	36.39	–
Citus oil	37.22	–
Cypress oil	39.57	–
Myrtle oil	40.32	–
Citronella oil	44.58	–
Vetiver bourbon oil	48.11	–
Marjoram oil	48.15	–
Lime oil	50.17	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33800	33800	0.00	20.54
34298	34298	0.00	17.84
34404	34404	0.00	17.21
33831	33831	0.00	20.48

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 2.3-2021-01

Validated substance/substance group	**Melissa oil 30%**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33812-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Melissa oil 30%; Melissa 30% (essential oil)

Special notes

When selecting the *Melissa oil 30%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Melissa oil 30%	2	1	0

Second-stage model

For differentiation of the substance/substance group *Melissa oil 30%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Melissa oil 30%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Melissa oil 30%	01029J25	33812	40	not required
Primavera	Melissa oil 30%	00344A26	33962	40	not required

Validation samples

A total of 53 906 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 *Melissa oil 30%*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 30 spectra of 1 reference samples from the substance/substance group *Melissa oil 30%*.
- 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
Primavera	Melissa oil 30%	00362G26	34297	30

- 20 771 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Melissa oil 30%*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Melissa oil 30%* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Melissa oil 30%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	30	0	20 771
Type C	0	0	0	8600

The substance/substance group *Melissa oil 30%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9462 %)	100.0000 % (> 80.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Melissa oil 30%* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Petitgrain oil	27.26	–
Neroli oil	31.62	–
Thyme oil, white	37.77	–
Lavender oil	40.59	–
Coriander oil	43.82	–
Spearmint oil	46.52	–
Juniper oil	47.75	–
Matricaria oil, morrocan	50.30	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Melissa oil 30%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33812	33812	0.00	27.26
33962	33962	0.00	30.25

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 2.3-2021-01

Validated substance/substance group	**Myrrh oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30748-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Myrrh oil; Oleum myrrha

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Myrrh oil	3	2	4

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Myrrh oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Myrrh oil	30007-120958	31692	60	not required
Taoasis	Myrrh oil	41197-124418BAG90451	32271	40	not required
Taoasis	Myrrh oil	2206-2428	33992	40	not required

Validation samples

A total of 53 906 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 *Myrrh oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Myrrh oil*.
- 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
Taoasis	Myrrh oil	22920-105398BAG90451	30748	40
Taoasis	Myrrh oil	41197-126694	33050	40
Taoasis	Myrrh oil	41197-126694	33051	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 4 batches from the substance/substance group *Myrrh oil*.

- 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
Taoasis	Myrrh oil	2067-107953	1
Taoasis	Myrrh oil	2206-1873	2
Taoasis	Myrrh oil	2379-6234	1
Taoasis	Myrrh oil	17F02206-4099	1

- 8595 spectra from 736 *Apo-Ident* customers from a total of 3542 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Myrrh oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Myrrh oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	79	41	20 681
Type C	0	4	1	8595

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9455 %)	65.8333 % (> 63.3333 %)
Type C	100.0000 % (> 98.7978 %)	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 *Myrrh oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Orange oil	49.81	–
Grapefruit oil, organic	52.92	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32271	32271	0.00	155.62
33992	33992	0.00	44.63
31692	31692	0.00	112.27

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 2.3-2021-01

Validated substance/substance group	**Neroli oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31260-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Neroli oil; Oleum neroli

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Neroli oil	4	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Neroli oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Neroli oil	00237B27	34406	40	not required
Taoasis	Neroli oil	91029-115714	31260	40	not required
Taoasis	Neroli oil	6142-120057BAG90451	31695	60	not required
Taoasis	Neroli oil	0717/4-3018	34283	40	not required

Validation samples

A total of 53 906 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 *Neroli oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 325 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Neroli oil*.
- 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
Taoasis	Neroli oil	125052-124958	32805	40
Taoasis	Neroli oil	071704-1966	33993	40
Taoasis	Neroli oil	125052-124958	33042	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Neroli oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Neroli oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Neroli oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	40	80	20 681
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9455 %)	33.3333 % (> 30.8333 %)
Type C	100.0000 % (> 98.8097 %)	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 *Neroli oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Coriander oil	32.21	–
Thyme oil, white	38.29	–
Lavender oil	42.96	–
Matricaria oil, morrocan	46.95	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31695	31695	0.00	50.82
31260	31260	0.00	47.00
34283	34283	0.00	53.69
34406	34406	0.00	42.96

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 2.3-2021-01

Validated substance/substance group	**Neuroderm® moisturising cream lipo**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30721-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Neuroderm® moisturising cream lipo

Special notes

When selecting the *Neuroderm® moisturising cream lipo* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Neuroderm® moisturising cream lipo	3	2	1

Second-stage model

For differentiation of the substance/substance group *Neuroderm® moisturising cream lipo* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Neuroderm® moisturising cream lipo*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Infectopharm	Neuroderm® moist…	S031202.1	30721	40	not required
Infectopharm	Neuroderm® moist…	S031506.1	31672	60	not required
Infectopharm	Neuroderm® moist…	S051723.1	34045	40	not required

Validation samples

A total of 53 906 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 *Neuroderm® moisturising cream lipo*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Neuroderm® moisturising cream lipo*.
- 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
Infectopharm	Neuroderm® moisturising crea…	S071617.2	32739	40
Infectopharm	Neuroderm® moisturising crea…	S021706.1	33287	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Neuroderm® moisturising cream lipo*.

- 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
Infectopharm	Neuroderm® moisturising crea…		1
Infectopharm/AHD	Neuroderm® moisturising crea…		1

- 8598 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Neuroderm® moisturising cream lipo* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Neuroderm® moisturising cream lipo* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	2	0	8598

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8173 %)	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 *Neuroderm® moisturising cream lipo* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dermatest base ointment	24.45	–
Lipolotio urea 5% F body lotion	24.60	–
Allergika evening primrose oil cream 20%	53.08	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30721	30721	0.00	30.86
31672	31672	0.00	24.40
34045	34045	0.00	30.54

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 2.3-2021-01

Validated substance/substance group	**Nicotine**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31019-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Nicotine

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Nicotine	3	1	0

Second-stage model

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

no second-stage model

Calibration samples

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

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Roth	Nicotine	152183017	31019	20	1402687
Roth	Nicotine	194210173	31508	60	1410523
Roth	Nicotine	194210173	31518	60	not required
Roth	Nicotine	116210173	31948	45	not required

Validation samples

A total of 53 906 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 *Nicotine*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 320 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Nicotine*.
- 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
Roth	Nicotine	137210173	33291	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Nicotine*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Nicotine* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Nicotine* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 320
Type B	0	40	0	20 761
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.7568 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Nicotine* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dichloroacetic acid	153.65	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31019	31019	0.00	170.06
31508	31508	0.00	168.74
31518	31518	0.00	169.05
31948	31948	0.00	169.65

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 2.3-2021-01

Validated substance/substance group	**Ointment ash basis / Neribas®**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30774-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ointment ash basis / Neribas®; Asche Basis® ointment; Neribas® ointment

Special notes

When selecting the *Ointment ash basis / Neribas®* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Asche Basis® ointment	1	2	49
Neribas® ointment	2	2	52

Second-stage model

For differentiation of the substance/substance group *Ointment ash basis / Neribas®* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ointment ash basis / Neribas®*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Chiesi	Asche Basis® oin…	21038A	30774	40	not required
Chiesi	Asche Basis® oin…	21038A	30833	40	not required
Chiesi	Asche Basis® oin…	21038A	31080	40	not required
Bayer	Neribas® ointment	21053B	30969	40	not required
Bayer	Neribas® ointment	21053B	30994	40	not required
Jenapharm	Neribas® ointment	31064C	31093	40	not required

Validation samples

A total of 53 906 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 *Ointment ash basis / Neribas®*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.

- 24 265 spectra from a total of 501 batches from further 159 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ointment ash basis / Neribas®*.

- 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
Chiesi	Asche Basis® ointment	61067A	32590	40
Chiesi	Asche Basis® ointment	17072A	33840	40
Jenapharm	Neribas® ointment	YY00TJ0	32564	40
Jenapharm	Neribas® ointment	YY016EC	33288	40
Chiesi	Asche Basis® ointment	61067A	32924	40
Chiesi	Asche Basis® ointment	61067A	32927	40

- 20 561 spectra from a total of 443 batches from further 202 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 57 *Apo-Ident* customers from 101 batches from the substance/substance group *Ointment ash basis / Neribas®*.

- Among them are spectra of independent samples from 100 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	Asche Basis® ointment	92083A	1
Anzag/Ichtyol-Gesellsch...	Asche Basis® ointment	23043A	1
Caelo	Asche Basis® ointment	31047A	1
Caelo	Asche Basis® ointment	81708A	1
Chiese	Asche Basis® ointment	63069A	1
Chiese	Asche Basis® ointment	63070A	1
Chiese	Asche Basis® ointment	71073A	2
Chiese/Sanacorp WE:07.0...	Asche Basis® ointment	52062A	1
chiesi	Asche Basis® ointment	42055A	1
chiesi	Asche Basis® ointment	44057A	1
Chiesi	Asche Basis® ointment	32048A	1
Chiesi	Asche Basis® ointment	33049A	1
Chiesi	Asche Basis® ointment	34051A	1
Chiesi	Asche Basis® ointment	41054A	3
Chiesi	Asche Basis® ointment	41052A	1
Chiesi	Asche Basis® ointment	51060A	1
Chiesi	Asche Basis® ointment	510604	1
Chiesi	Asche Basis® ointment	52063A	3
Chiesi	Asche Basis® ointment	52062A	3
Chiesi	Asche Basis® ointment	53065A	2
Chiesi	Asche Basis® ointment	63069A	3
Chiesi	Asche Basis® ointment	63068A	1
Chiesi	Asche Basis® ointment	83079A	1
Chiesi	Asche Basis® ointment	83080A	1
Chiesi / Gehe	Asche Basis® ointment	33049A	1
Chiesi / Gehe	Asche Basis® ointment	33050A	1
Chiesi / Phönix	Asche Basis® ointment	91082A	1
Chiesi / Phönix	Asche Basis® ointment	92083A	1
Chiesi / Phönix	Asche Basis® ointment	83080A	1
Chiesi / Sanacorp	Asche Basis® ointment	92084A	1
chiesi /Gehe	Asche Basis® ointment	73075A	1
Chiesi Gmbh	Asche Basis® ointment	21039A	1

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Supplier	Substance	Batch	Spectra
Chiesi GmbH	Asche Basis® ointment	52062A	1
Chiesi GmbH	Asche Basis® ointment	52064A	3
Chiesi GmbH	Asche Basis® ointment	53065A	4
Chiesi GmbH	Asche Basis® ointment	61066A	2
Chiesi GmbH	Asche Basis® ointment	63070A	2
Chiesi GmbH	Asche Basis® ointment	71071A	1
Chiesi GmbH	Asche Basis® ointment	71072A	1
Chiesi GmbH	Asche Basis® ointment	71073A	1
Chiesi GmbH	Asche Basis® ointment	72074A	1
Chiesi GmbH / Sanacorp	Asche Basis® ointment	92034A	1
Chiesi/ Anzag	Asche Basis® ointment	83079A	1
CHIESI/ NOWEDA	Asche Basis® ointment	51060A	2
Chiesi/AHD	Asche Basis® ointment	31045A	4
Chiesi/AHD	Asche Basis® ointment	31047A	1
Chiesi/AHD	Asche Basis® ointment	33049A	1
Chiesi/Alliance	Asche Basis® ointment	61067A	1
Chiesi/Anzag	Asche Basis® ointment	1(92084A)	1
chiesi/gehe	Asche Basis® ointment	71072A	1
Chiesi/Gehe	Asche Basis® ointment	42056A	1
Chiesi/Gehe	Asche Basis® ointment	83079A	1
Chiesi/Gehe	Asche Basis® ointment	92085A	1
Chiesi/Jenne	Asche Basis® ointment	73076A	1
Chiesi/Jenne	Asche Basis® ointment	74077A	2
Chiesi/Krieger	Asche Basis® ointment	61066A	1
Chiesi/Noweda	Asche Basis® ointment	71072A	1
Chiesi/Phoenix	Asche Basis® ointment	23042A	1
Chiesi/Phoenix	Asche Basis® ointment	73076A	1
Chiesi/Phoenix	Asche Basis® ointment	73075A	1
Chiesi/Phönix	Asche Basis® ointment	51059A	1
Chiesi/Phönix	Asche Basis® ointment	71073A	1
Chiesi/Phönix	Asche Basis® ointment	72074A	2
Chiesi/Phönix	Asche Basis® ointment	81078A	1
Chiesi/Phönix	Asche Basis® ointment	83079A	2
Chiesi/Phönix	Asche Basis® ointment	84081A	2
Chiesi/Sanacorp	Asche Basis® ointment	41053A	1
Chiesi/Sanacorp	Asche Basis® ointment	71072A	1
Chiesi/Sanacorp	Asche Basis® ointment	83080A	1
Chieso	Asche Basis® ointment	52063A	2
Gehe	Asche Basis® ointment	17I21-B01	1
Caelo	Asche Basis® ointment	63068A	3
Caelo	Asche Basis® ointment	61067A	1
Noweda	Asche Basis® ointment	71072A	1
Noweda	Asche Basis® ointment	84081A	1
Noweda	Asche Basis® ointment	83080A	1
Noweda	Asche Basis® ointment	2088A	1
Noweda	Asche Basis® ointment	2089A	2
Noweda	Asche Basis® ointment	92085A	1
Phönix	Asche Basis® ointment	31047A	1
PPL	Asche Basis® ointment	61067A	1
PPL	Asche Basis® ointment	71072A	2
PPL	Asche Basis® ointment	73075A	1
Sanacorp WE 29.04.17 -8...	Asche Basis® ointment	63070A	1
Sanacorp/Chiesi WE:31.0...	Asche Basis® ointment	41054A	1
SanacorpWE:9.12.2016 ...	Asche Basis® ointment	63068A	1
WE:27.02.2016 Sanacor...	Asche Basis® ointment	52063A	1
WE:Sanacorp19.01.2016 ...	Asche Basis® ointment	52064A	2
WE14.12.16 Chiesi/Sanac...	Asche Basis® ointment	61067A	2
Wolff/AHD	Asche Basis® ointment	32048A	2
Audor Pharma	Neribas® ointment	YY02825	1
Bayer	Neribas® ointment	YY01KHH	1

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Supplier	Substance	Batch	Spectra
Bayer/ Sanacorp	Neribas® ointment	YY006JT	3
Bayer/Sanacorp	Neribas® ointment	YY00THL	1
Caelo	Neribas® ointment	YY016EC	1
Caelo	Neribas® ointment	YY00TJ0	1
Caelo	Neribas® ointment	YY00XEH	1
Caelo	Neribas® ointment	YY016LN	1
Caelo	Neribas® ointment	YY00CC8	1
Caelo	Neribas® ointment	YY00THL	2
Gehe	Neribas® ointment	YY023JE	1
Jenaparm	Neribas® ointment	12091812	1
Jenapharm	Neribas® ointment	YY006JT	1
Jenapharm	Neribas® ointment	YY00XEH	1
Jenapharm	Neribas® ointment	YY016LN	2
Jenapharm	Neribas® ointment	YY00TJ0	1
Jenapharm	Neribas® ointment	YY016EC	1
Jenapharm	Neribas® ointment	YY017LF	1
Jenapharm	Neribas® ointment	YY01FX4	3
Jenapharm	Neribas® ointment	YY01KHH	1
Jenapharm	Neribas® ointment	YY01TF3	1
Jenapharm	Neribas® ointment	5121811	1
Jenapharm	Neribas® ointment	YY02825	4
Jenapharm	Neribas® ointment	YY02L88	2
Jenapharm / Anzag	Neribas® ointment	YY00THL	1
Jenapharm / Anzag	Neribas® ointment	75(YY02825)	1
Jenapharm / Anzag	Neribas® ointment	76(YY02825)	1
Jenapharm / Anzag	Neribas® ointment	80(YY02L27)	1
Jenapharm / Anzag	Neribas® ointment	84(YY02L88)	1
Jenapharm Anzag	Neribas® ointment	70(YY01YEX)	1
Jenapharm Anzag	Neribas® ointment	71(YY023J1)	1
Jenapharm Anzag	Neribas® ointment	72(YY02835)	1
Jenapharm Anzag	Neribas® ointment	81(YY02L27)	1
Jenapharm Anzag	Neribas® ointment	82(YY02L88)	1
Jenapharm Anzag	Neribas® ointment	83(YY02L88)	1
Jenapharm GmbH	Neribas® ointment	YY019PE	1
Jenapharm/ Anzag	Neribas® ointment	YY00K7E	2
Jenapharm/ Anzag	Neribas® ointment	77(YY02825)	1
Jenapharm/ Anzag	Neribas® ointment	78(YY02L27)	1
Jenapharm/ Anzag	Neribas® ointment	79(YY02L27)	1
Jenapharm/ Gehe	Neribas® ointment	YY01TF3	2
Jenapharm/ Gehe	Neribas® ointment	YY023J1	1
Jenapharm/ Gehe	Neribas® ointment	YY02825	3
Jenapharm/ Gehe	Neribas® ointment	YY02L27	2
Jenapharm/ Gehe	Neribas® ointment	YY02L88	1
Jenapharm/ Sanacorp	Neribas® ointment	YY00THL	1
Jenapharm/AHD	Neribas® ointment	58(YY0180C)	1
Jenapharm/AHD	Neribas® ointment	59(YY01KHH)	1
Jenapharm/AHD	Neribas® ointment	58(YY01FX4)	1
Jenapharm/AHD	Neribas® ointment	62(YY01KHH)	1
Jenapharm/AHD	Neribas® ointment	61(YY01KHH)	1
Jenapharm/AHD	Neribas® ointment	60(YY01KHH)	2
Jenapharm/AHD	Neribas® ointment	65(YY019PE)	1
Jenapharm/AHD	Neribas® ointment	67(YY01TF3)	1
Jenapharm/AHD	Neribas® ointment	66(YY01TF3)	1
Jenapharm/AHD	Neribas® ointment	68(YY01YEX)	1
Jenapharm/Alliance	Neribas® ointment	YY016EC	1
Jenapharm/Anzag	Neribas® ointment	YY00XEH	2
Jenapharm/Anzag	Neribas® ointment	69(YY01YEX)	1
Jenapharm/Gehe	Neribas® ointment	YY01YEX	1
Jenapharm/Gehe	Neribas® ointment	YY01FX4	1
Jenapharm/Gehe	Neribas® ointment	YY023JE	1

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Supplier	Substance	Batch	Spectra
Jenapharm/Jenne	Neribas® ointment	61(YY019PE)	1
Jenapharm/Jenne	Neribas® ointment	YY01TF3	1
Jenapharm/Noweda	Neribas® ointment	YY00THL	1
Jenapharm/Phoenix	Neribas® ointment	YY023JE	1
Jenapharm/Phönix	Neribas® ointment	YY006JT	1
Jenapharm/Phönix	Neribas® ointment	YY01KHH	1
Jenapharm/Sanacorp	Neribas® ointment	YY0180C	1
Leo Pharma / Phönix	Neribas® ointment	YY0431X	1
LeoPharm/Alliance	Neribas® ointment	YY01FX4	1
Leopharma/Jenne	Neribas® ointment	YY02L88	3
Phönix	Neribas® ointment	YY0431Y	1
Römer/apo	Neribas® ointment	YY008RJ	1
Wolf Apotheke	Neribas® ointment	73(YY02825)	1
Wolf Apotheke	Neribas® ointment	74(YY02825)	1
Chiesi/Jenne	Asche Basis® ointment		1

- 8381 spectra from 735 *Apo-Ident* customers from a total of 3445 batches from a further 148 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ointment ash basis / Neribas®* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ointment ash basis / Neribas®* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 265
Type B	0	240	0	20 481
Type C	0	204	15	8381

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 98.7851 %)	93.1507 % (> 91.7808 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Ointment ash basis / Neribas®* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Bepanthen® Wund- und Heilsalbe	23.96	–
Alfason Basis Cresa®	26.20	–
Linola® fat cream	56.85	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30969	30969	0.00	38.08
30994	30994	0.00	34.59
31093	31093	0.00	30.58
30774	30774	0.00	33.96
30833	30833	0.00	35.84
31080	31080	0.00	33.31

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 2.3-2021-01

Validated substance/substance group	**Orange aroma**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31190-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Orange aroma; Orange flavour

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Orange aroma	5	6	57

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Orange aroma*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Orange aroma	13123307	31190	40	not required
Caelo	Orange aroma	13406108	31402	40	not required
Caelo	Orange aroma	163470	33100	40	20161221*
Fagron	Orange aroma	13H23-B41-295530	31510	60	not required
Fagron	Orange aroma	18I17-B06-366492	35087	40	not required

Validation samples

A total of 53 906 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 *Orange aroma*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.
- 24 285 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Orange aroma*.
- 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	Orange aroma	162063	32331	40
Caelo	Orange aroma	173005	33881	40
Caelo	Orange aroma	180831	34076	40
Caelo	Orange aroma	182057	34224	40
Caelo	Orange aroma	183261	34323	40
Caelo	Orange aroma	190933	34629	40

- 20 561 spectra from a total of 441 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 251 spectra from 137 *Apo-Ident* customers from 59 batches from the substance/substance group *Orange aroma*.
- Among them are spectra of independent samples from 57 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Allergika/Kehr	Orange aroma	16056107	1
Audor Pharma	Orange aroma	15215409	1
Caelo	Orange aroma	23051201	1
Caelo	Orange aroma	12216712	2
Caelo	Orange aroma	12356503	2
Caelo	Orange aroma	25031304	1
Caelo	Orange aroma	13330206	1
Caelo	Orange aroma	13406104	1
Caelo	Orange aroma	14150707	4
Caelo	Orange aroma	15215402	4
Caelo	Orange aroma	15215403	2
Caelo	Orange aroma	15215410	1
Caelo	Orange aroma	16056105	9
Caelo	Orange aroma	16206301	3
Caelo	Orange aroma	16056108	1
Caelo	Orange aroma	17055104	1
Caelo	Orange aroma	17055110	1
Caelo	Orange aroma	17300509	7
Caelo	Orange aroma	18205701	11
Caelo	Orange aroma	19093301	8
Caelo	Orange aroma	19093312	2
Caelo	Orange aroma	19093311	6
Caelo	Orange aroma	92968005	1
Caelo	Orange aroma	192968005	1
Caelo	Orange aroma	14150706	4
Caelo	Orange aroma	19093307	4
Caelo	Orange aroma	17300507	9
Caelo	Orange aroma	19093302	1
Caelo	Orange aroma	18083103	9
Caelo	Orange aroma	14150714	2
Caelo	Orange aroma	20000419006	5
Caelo	Orange aroma	18205702	1

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Supplier	Substance	Batch	Spectra
Caelo	Orange aroma	19093309	1
Caelo	Orange aroma	14352903	1
Caelo	Orange aroma	18326113	7
Caelo	Orange aroma	16347012	1
Caelo	Orange aroma	15215401	2
Caelo	Orange aroma	20000419003	1
Caelo	Orange aroma	192968003	9
Caelo	Orange aroma	17300501	8
Caelo	Orange aroma	12356502	1
Caelo	Orange aroma	13123305	2
Caelo	Orange aroma	13406101	2
Caelo	Orange aroma	14352904	3
Caelo	Orange aroma	15215408	4
Caelo	Orange aroma	16347005	10
Caelo	Orange aroma	160566107	1
Caelo	Orange aroma	17055103	2
Caelo	Orange aroma	18326108	5
Caelo	Orange aroma	16056107	5
Caesar & Loretz GmbH	Orange aroma	18205701	1
Caesar & Loretz GmbH	Orange aroma	18083103	1
Caesar & Loretz GmbH	Orange aroma	18326103	7
Caesar & Loretz GmbH	Orange aroma	17300509	1
Caesar & Loretz GmbH	Orange aroma	18326113	3
Caesar & Loretz GmbH	Orange aroma	19093301	1
Caesar & Loretz GmbH	Orange aroma	19093307	1
Caesar & Loretz GmbH	Orange aroma	19093311	3
Caesar & Loretz GmbH	Orange aroma	20000419003	3
Caesar & Loretz GmbH	Orange aroma	20000419007	2
Caesar & Loretz GmbH	Orange aroma	20000419012	1
Caesar & Loretz GmbH	Orange aroma	20000419006	1
Caesar & Loretz GmbH / …	Orange aroma	16347005	1
Caesar & Loretz GmbH/Gehe	Orange aroma	19093311	1
Caesar & Loretz GmbH/Kehr	Orange aroma	18326103	1
Caesar & Loretz GmbH/Kehr	Orange aroma	20000419006	1
Caesar&Loretz GmbH/ San…	Orange aroma	17300501	1
Caesar&Loretz GmbH/ San…	Orange aroma	19093301	1
Euro OTC	Orange aroma	17055103	1
Fagron	Orange aroma	17A30-B02-335197	1
Fagron	Orange aroma	17300507	1
Gehe	Orange aroma	16056107	1
Gehe	Orange aroma	18326108	1
GEHE	Orange aroma	17300507	1
Caelo	Orange aroma	14352906	2
Caelo	Orange aroma	18326103	21
Henry LamotteOlis GmbH	Orange aroma	18205701	1
Caelo	Orange aroma	13123309	2
Caelo	Orange aroma	13330207	1
Caelo	Orange aroma	14150703	1
Phoenix	Orange aroma	17300509	3
Phoenix	Orange aroma	18326103	2
Phönix	Orange aroma	18083103	1
Phönix 17.1.19	Orange aroma	18083103	1
Sanacorp	Orange aroma	12356503	1
Sanacorp	Orange aroma	17300507	1
Fagron	Orange aroma	14352904	1
	Orange aroma	17300501	1
Caelo	Orange aroma	13406108	2
Caelo	Orange aroma		1

- 8349 spectra from 725 *Apo-Ident* customers from a total of 3487 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Orange aroma* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Orange aroma* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 285
Type B	0	240	0	20 561
Type C	0	249	2	8349

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 97.5000 %)
Type C	100.0000 % (> 98.7850 %)	99.2032 % (> 98.0080 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Ethanol 70% pure / denatured	35.76	–

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31510	31510	0.00	107.01
31190	31190	0.00	59.89
31402	31402	0.00	60.15
33100	33100	0.00	62.35
35087	35087	0.00	101.77

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 2.3-2021-01

Validated substance/substance group	**Oregano oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31554-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Oregano oil; Oleum origani cretici

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Oregano oil	5	1	1

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Oregano oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Oregano oil	00256M26	34368	40	not required
Taoasis	Oregano oil	0131022-117999	31554	60	not required
Taoasis	Oregano oil	7921018-119483	31779	60	not required
Taoasis	Oregano oil	43878A-125814	32769	40	not required
Taoasis	Oregano oil	44314A-129096	33649	40	not required

Validation samples

A total of 53 906 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 *Oregano oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.

- 24 265 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Oregano oil*.

- 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
Taoasis	Oregano oil	43878A-123201	32939	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Oregano oil*.

- 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
Taoasis/Gehe	Oregano oil	6553TR-L03	1

- 8599 spectra from 736 *Apo-Ident* customers from a total of 3545 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Oregano oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Oregano oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 265
Type B	0	40	0	20 761
Type C	0	1	0	8599

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8499 %)	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 *Oregano oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Thyme oil, red	33.22	–
Savory herb	66.10	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31779	31779	0.00	139.87
31554	31554	0.00	96.45
32769	32769	0.00	48.70
33649	33649	0.00	51.54
34368	34368	0.00	69.59

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 2.3-2021-01

Validated substance/substance group	**Palmarosa oil, organic**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30597-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Palmarosa oil, organic; Oleum palmarosae

Special notes

When selecting the *Palmarosa oil, organic* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Palmarosa oil, organic	3	3	5

Second-stage model

For differentiation of the substance/substance group *Palmarosa oil, organic* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Palmarosa oil, organic*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Palmarosa oil, o…	2461021-121891	31828	60	not required
Taoasis	Palmarosa oil, o…	4941003-126708	33043	40	not required
Taoasis	Palmarosa oil, o…	2141-3447	34289	40	not required

Validation samples

A total of 53 906 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 *Palmarosa oil, organic*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Palmarosa oil, organic*.
- 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
Primavera	Palmarosa oil, organic	00500L26	34366	40
Taoasis	Palmarosa oil, organic	17524-105015BAG90451	30597	40
Taoasis	Palmarosa oil, organic	104704-129227	33856	40

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Supplier	Substance	Batch	Sample ID	Spectra
Taoasis	Palmarosa oil, organic	17524-105015BAG90451	30671	40
Taoasis	Palmarosa oil, organic	4941003-126708	33044	40

- 20 601 spectra from a total of 443 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 5 *Apo-Ident* customers from 5 batches from the substance/substance group *Palmarosa oil, organic*.

- 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
Taoasis	Palmarosa oil, organic	121018-111094	1
Taoasis	Palmarosa oil, organic	121018-111872	2
Taoasis	Palmarosa oil, organic	2242	1
Taoasis GmbH/ Taoasis	Palmarosa oil, organic	2587-7434	1
Taoasis/Taoasis	Palmarosa oil, organic	121018-111872	1
Taoasis/Taoasis	Palmarosa oil, organic	2215-5590	1

- 8593 spectra from 736 *Apo-Ident* customers from a total of 3541 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Palmarosa oil, organic* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Palmarosa oil, organic* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	200	0	20 601
Type C	0	7	0	8593

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.7941 %)	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 *Palmarosa oil, organic* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Marjoram oil	96.13	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31828	31828	0.00	123.69
34289	34289	0.00	116.13
33043	33043	0.00	107.92

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 2.3-2021-01

Validated substance/substance group	**Panthenol ointment Lichtenstein**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30727-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Panthenol ointment Lichtenstein

Special notes

When selecting the *Panthenol ointment Lichtenstein* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Panthenol ointment Lichtenstein	3	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Panthenol ointment Lichtenstein*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Winthrop	Panthenol ointme…	2290680H	30727	40	not required
Winthrop	Panthenol ointme…	2290718H	31091	40	not required
Zentiva Pharm…	Panthenol ointme…	EH4594	31764	60	not required

Validation samples

A total of 53 906 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 *Panthenol ointment Lichtenstein*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.

- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Panthenol ointment Lichtenstein*.

- 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
Zentiva Pharma GmbH	Panthenol ointment Lichtenst…	GC5567	33284	40
Zentiva Pharma GmbH	Panthenol ointment Lichtenst…	GD5661	33425	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Panthenol ointment Lichtenstein*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Panthenol ointment Lichtenstein* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Panthenol ointment Lichtenstein* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Panthenol ointment Lichtenstein* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
La Roche-Posay Cold Cream Naturel	100.86	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31764	31764	0.00	157.21
31091	31091	0.00	186.24
30727	30727	0.00	189.25

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 2.3-2021-01

Validated substance/substance group	**Patchouli oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31547-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Patchouli oil; Oleum pogostemon cablin

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Patchouli oil	3	3	2

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Patchouli oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Patchouli oil	14167204	31619	60	not required
Taoasis	Patchouli oil	130930-112789	31547	60	not required
Taoasis	Patchouli oil	FFL735-123003	32172	40	not required

Validation samples

A total of 53 906 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 *Patchouli oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Patchouli oil*.
- 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
Primavera	Patchouli oil	00475B27	34389	40
Taoasis	Patchouli oil	1633-126207	33031	40
Taoasis	Patchouli oil	P29-1186	34113	40
Taoasis	Patchouli oil	1633-126207	33032	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Patchouli oil*.

- 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
Taoasis	Patchouli oil	130930-116684	1
Taoasis	Patchouli oil	33474-119161	1

- 8598 spectra from 736 *Apo-Ident* customers from a total of 3544 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Patchouli oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Patchouli oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	73	87	20 641
Type C	0	1	1	8598

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9454 %)	45.6250 % (> 43.7500 %)
Type C	100.0000 % (> 98.8173 %)	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 *Patchouli oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lemon grass oil	23.68	–
Marjoram oil	25.61	–
Carrot seed oil	29.44	–
Tea tree oil	29.55	–
Cedar wood oil	32.80	–
Immortelle oil	44.78	–
Cypress oil	50.46	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31619	31619	0.00	35.94
32172	32172	0.00	36.03
31547	31547	0.00	23.68

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 2.3-2021-01

Validated substance/substance group	**Peppermint oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30930-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Peppermint oil; Oleum menthae piperitae dopp. rectific.

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Peppermint oil	4	5	65

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Peppermint oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Peppermint oil	00098J25	33809	40	not required
Taoasis	Peppermint oil	443428-83579	30930	40	not required
Taoasis	Peppermint oil	525728-109217B	30965	40	not required
Taoasis	Peppermint oil	2016104277-125426	32481	40	not required

Validation samples

A total of 53 906 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 *Peppermint oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 345 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Peppermint oil*.
- 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
Primavera	Peppermint oil	00374B26	33958	40

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Supplier	Substance	Batch	Sample ID	Spectra
Primavera	Peppermint oil	00221G26	34168	40
Primavera	Peppermint oil	00465A27	34371	40
Taoasis	Peppermint oil	2016104277-126375	32804	40
Taoasis	Peppermint oil	104277-126684	33030	40

- 20 601 spectra from a total of 442 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 103 spectra from 70 *Apo-Ident* customers from 66 batches from the substance/substance group *Peppermint oil*.

- 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
Bombastus	Peppermint oil	286204	1
Bombastus	Peppermint oil	18003695	2
Bombastus	Peppermint oil	307854	3
Bombastus	Peppermint oil	180051143413	1
Bombastus	Peppermint oil	18006685	4
Bombastus	Peppermint oil	20001977	1
Bombastus	Peppermint oil	18005114	2
Caelo	Peppermint oil	12114225	1
Caelo	Peppermint oil	15255818	1
Caelo	Peppermint oil	16114611	1
Caelo	Peppermint oil	16114630	1
Caelo	Peppermint oil	17188612	1
Caelo	Peppermint oil	17291901	1
Caelo	Peppermint oil	1703032-01	1
Caelo	Peppermint oil	18003695	1
Caelo	Peppermint oil	18208412	1
Caelo	Peppermint oil	18221712	3
Caelo	Peppermint oil	18208405	1
Caelo	Peppermint oil	19135908	1
Caelo	Peppermint oil	191359007	2
Caelo	Peppermint oil	18221701	2
Caelo	Peppermint oil	18208401	1
Caelo	Peppermint oil	18221716	6
Caelo	Peppermint oil	17364301	1
Caelo	Peppermint oil	9135901	1
Caelo	Peppermint oil	617Q-01995	1
Caelo	Peppermint oil	1319I-01995	1
Caelo	Peppermint oil	17188609	3
Caelo	Peppermint oil	191136001	1
Caelo	Peppermint oil	19135902	1
Caelo	Peppermint oil	18221702	4
Caelo	Peppermint oil	18221723	3
Euro OTC	Peppermint oil	16114611	1
Euro OTC	Peppermint oil	1804008-01	1

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Supplier	Substance	Batch	Spectra
Euro OTC	Peppermint oil	180400802	1
Fagron	Peppermint oil	19F01-803	1
Fagron	Peppermint oil	19C14-B12-191227	1
Fagron	Peppermint oil	19j21-b14-193446	1
Fagron	Peppermint oil	15B11-B08-304117	1
Bombastus	Peppermint oil	19004746	1
Gehe	Peppermint oil	17F08-B07-339333	1
Gehe	Peppermint oil	18221716	1
Kögl	Peppermint oil	421211154615	1
Melsan	Peppermint oil	1705811	1
Ph/Euro	Peppermint oil	170303202	1
Phoenix	Peppermint oil	19135905	1
Phoenix 28.12..18	Peppermint oil	18221702	1
Caelo	Peppermint oil	19135905	2
Primavera	Peppermint oil	61M27	1
Taoasis	Peppermint oil	24699-117643	1
Taoasis	Peppermint oil	40076-120885	1
Taoasis	Peppermint oil	41798-121607	1
Taoasis	Peppermint oil	63561-125729	1
Taoasis	Peppermint oil	63561-126008	2
Taoasis	Peppermint oil	63561-125104	1
Taoasis	Peppermint oil	52216-123564	1
Taoasis	Peppermint oil	65074-125102BAG90451	1
Taoasis	Peppermint oil	75404-127882	1
Taoasis	Peppermint oil	79725-126853	1
Taoasis	Peppermint oil	79725-12653	1
Taoasis	Peppermint oil	78725-128653	1
Taoasis	Peppermint oil	79725-128653	2
Taoasis	Peppermint oil	88914-2568	1
Taoasis	Peppermint oil	93360-3339	4
Taoasis	Peppermint oil	1800141-3963	1
Taoasis	Peppermint oil	111455-6397	3
Taoasis/ Kehr	Peppermint oil	41798-120746H08	1
Taoasis/Kehr	Peppermint oil	127711	1
TAOASIS/phönix	Peppermint oil	7308L09-CN	1
Taoasis/Taoasis	Peppermint oil	41798-12517	1
Toasis/Noweda	Peppermint oil		2

- 8497 spectra from 731 *Apo-Ident* customers from a total of 3481 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Peppermint oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Peppermint oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	190	10	20 601
Type C	0	99	4	8497

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9454 %)	95.0000 % (> 93.5000 %)
Type C	100.0000 % (> 98.7854 %)	96.1165 % (> 93.2039 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Carrot seed oil	67.50	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30930	30930	0.00	87.58
30965	30965	0.00	93.78
32481	32481	0.00	72.51
33809	33809	0.00	69.08

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 2.3-2021-01

Validated substance/substance group	**Perfume oil vanilla**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30665-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Perfume oil vanilla; Oleum vanillae planifoliae

Special notes

When selecting the *Perfume oil vanilla* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Perfume oil vanilla	3	1	2

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Perfume oil vanilla*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Perfume oil vani…	10293212	30665	40	not required
Caelo	Perfume oil vani…	13393501	31191	40	1403100
Caelo	Perfume oil vani…	13393501	31400	40	not required
Caelo	Perfume oil vani…	14284107	31786	60	not required

Validation samples

A total of 53 906 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 *Perfume oil vanilla*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 325 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Perfume oil vanilla*.
- 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	Perfume oil vanilla	15316308	33439	40
Caelo	Perfume oil vanilla	15316308	33440	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 2 batches from the substance/substance group *Perfume oil vanilla*.

- 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	Perfume oil vanilla	15316308	12
Caelo	Perfume oil vanilla	17054404	2
Caesar & Loretz GmbH	Perfume oil vanilla	17054404	1

- 8585 spectra from 736 *Apo-Ident* customers from a total of 3544 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Perfume oil vanilla* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Perfume oil vanilla* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 325
Type B	0	80	0	20 721
Type C	0	15	0	8585

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.6667 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7891 %)	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 *Perfume oil vanilla* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Salmon oil	97.45	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30665	30665	0.00	124.58
31191	31191	0.00	121.70
31400	31400	0.00	122.39
31786	31786	0.00	130.78

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 2.3-2021-01

Validated substance/substance group	**Raspberry aroma**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30562-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Raspberry aroma; Raspberry flavour

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Raspberry aroma	3	4	62

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Raspberry aroma*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Raspberry aroma	12246612	31171	40	1402588
Caelo	Raspberry aroma	14115902	31396	40	not required
Caelo	Raspberry aroma	16126605	33222	40	not required

Validation samples

A total of 53 906 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 *Raspberry aroma*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 385 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Raspberry aroma*.
- 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	Raspberry aroma	12054307	30611	40
Caelo	Raspberry aroma	15438503	33054	40
Caelo	Raspberry aroma	172581	33697	40
Caelo	Raspberry aroma	192776	34746	40

- 20 641 spectra from a total of 443 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 125 *Apo-Ident* customers from 65 batches from the substance/substance group *Raspberry aroma*.

- 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	Raspberry aroma	12054311	1
Anzag06.	Raspberry aroma	14376109	1
Bombastus	Raspberry aroma	12246608	1
Caelo	Raspberry aroma	12246608	2
Caelo	Raspberry aroma	12054310	1
Caelo	Raspberry aroma	11303813	1
Caelo	Raspberry aroma	12246604	1
Caelo	Raspberry aroma	12054302	1
Caelo	Raspberry aroma	13255502	2
Caelo	Raspberry aroma	13255510	1
Caelo	Raspberry aroma	14376109	4
Caelo	Raspberry aroma	14376103	2
Caelo	Raspberry aroma	14376115	4
Caelo	Raspberry aroma	15219102	3
Caelo	Raspberry aroma	15438503	8
Caelo	Raspberry aroma	16126602	3
Caelo	Raspberry aroma	16126606	2
Caelo	Raspberry aroma	17187205	8
Caelo	Raspberry aroma	17187202	4
Caelo	Raspberry aroma	17187209	5
Caelo	Raspberry aroma	17258103	1
Caelo	Raspberry aroma	17258101	6
Caelo	Raspberry aroma	217258101	1
Caelo	Raspberry aroma	18074302	9
Caelo	Raspberry aroma	18249905	2
Caelo	Raspberry aroma	20002006003	1
Caelo	Raspberry aroma	192776	2
Caelo	Raspberry aroma	20002006002	1
Caelo	Raspberry aroma	192776010	1
Caelo	Raspberry aroma	19160006	2
Caelo	Raspberry aroma	18074307	13
Caelo	Raspberry aroma	17187201	1
Caelo	Raspberry aroma	15438501	8
Caelo	Raspberry aroma	18249907	3
Caelo	Raspberry aroma	12246616	2
Caelo	Raspberry aroma	16126609	5
Caelo	Raspberry aroma	13255507	2
Caelo	Raspberry aroma	192776006	1
Caelo	Raspberry aroma	192776002	1
Caelo	Raspberry aroma	13255514	2
Caelo	Raspberry aroma	17258102	5

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Supplier	Substance	Batch	Spectra
Caelo	Raspberry aroma	17258107	3
Caelo	Raspberry aroma	19160002	9
Caelo	Raspberry aroma	17187213	1
Caelo	Raspberry aroma	19160001	3
Caelo	Raspberry aroma	14115909	1
Caelo	Raspberry aroma	15219111	4
Caelo	Raspberry aroma	17187212	11
Caelo	Raspberry aroma	18074305	1
Caelo	Raspberry aroma	171872002	1
Caelo	Raspberry aroma	191600002	1
Caelo	Raspberry aroma	12246617	1
Caelo	Raspberry aroma	14115913	2
Caelo	Raspberry aroma	14115912	1
Caeolo	Raspberry aroma	14376103	1
Caesar & Loretz GmbH	Raspberry aroma	18074307	2
Caesar & Loretz GmbH	Raspberry aroma	18249907	1
Caesar & Loretz GmbH	Raspberry aroma	18249910	3
Caesar & Loretz GmbH	Raspberry aroma	18249912	3
Caesar & Loretz GmbH	Raspberry aroma	19160001	1
Caesar & Loretz GmbH	Raspberry aroma	18249911	1
Caesar & Loretz GmbH	Raspberry aroma	19160002	8
Caesar & Loretz GmbH	Raspberry aroma	19160008	1
Caesar & Loretz GmbH	Raspberry aroma	192776006	4
Caesar & Loretz GmbH	Raspberry aroma	20002006002	1
Caesar & Loretz GmbH / ...	Raspberry aroma	18249907	1
Caesar & Loretz GmbH/ AHD	Raspberry aroma	19160002	1
Caesar & Loretz GmbH/ G...	Raspberry aroma	18249902	1
Caesar & Loretz GmbH/Sa...	Raspberry aroma	19160001	1
Caesar/Noweda	Raspberry aroma	212m-07020	1
Fagron	Raspberry aroma	18074307	1
Fiebig	Raspberry aroma	192776006	1
Gehe	Raspberry aroma	19160002	1
Caelo	Raspberry aroma	18249910	1
Caelo	Raspberry aroma	18249912	2
Henry Lamotte/AHD	Raspberry aroma	17538106	1
Intern Drogen/Phoenix	Raspberry aroma	15438501	1
Kehr	Raspberry aroma	16126609	1
Kehr	Raspberry aroma	17187209	1
Noweda	Raspberry aroma	14115909	1
Noweda	Raspberry aroma	18249905	1
Caelo	Raspberry aroma	17258106	9
Phoenix	Raspberry aroma	17258106	1
Phoenix	Raspberry aroma	18249910	1
Phönix	Raspberry aroma	15438506	1
Phönix	Raspberry aroma	18249905	1
Phönix Gotha	Raspberry aroma	12246612	1
Rondell Apotheke	Raspberry aroma	15438501	1
Caelo	Raspberry aroma	16126611	3
Caelo	Raspberry aroma	12246612	1
Caelo	Raspberry aroma	16126605	6
Caelo	Raspberry aroma	14115902	1

- 8368 spectra from 720 *Apo-Ident* customers from a total of 3481 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Raspberry aroma* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Raspberry aroma* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	157	3	20 641
Type C	0	223	9	8368

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9454 %)	98.1250 % (> 96.2500 %)
Type C	100.0000 % (> 98.7851 %)	96.1207 % (> 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 *Raspberry aroma* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Contramarum aroma	58.73	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31171	31171	0.00	64.35
31396	31396	0.00	68.55
33222	33222	0.00	76.00

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 2.3-2021-01

Validated substance/substance group	**Ravensara oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30386-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ravensara oil; Ravensara (essentiel oil)

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Ravensara oil	2	3	14

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ravensara oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Ravensara oil	231012-118739	31635	60	not required
Taoasis	Ravensara oil	1687-966	33854	40	not required
Taoasis	Ravensara oil	1687-966	33872	40	not required

Validation samples

A total of 53 906 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 *Ravensara oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 365 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ravensara oil*.
- 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
Primavera	Ravensara oil	00065B27	34403	40
Taoasis	Ravensara oil	1687-125316	32803	40
Taoasis	Ravensara oil	1994-3103	34285	40
Taoasis	Ravensara oil	1687-125316	33029	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 15 batches from the substance/substance group *Ravensara oil*.
- 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
Taoasis	Ravensara oil	2101005-116830	3
Taoasis	Ravensara oil	231012-118738	1
Taoasis	Ravensara oil	231012-118892	1
Taoasis	Ravensara oil	9331006-121650	3
Taoasis	Ravensara oil	231012-120291	1
Taoasis	Ravensara oil	231012-119831	1
Taoasis	Ravensara oil	1687-125316	1
Taoasis	Ravensara oil	1687-127661	1
Taoasis	Ravensara oil	1687-126824	1
Taoasis	Ravensara oil	59/144/17	1
Taoasis	Ravensara oil	1944-1733	1
Taoasis	Ravensara oil	1994-3103	1
Taoasis	Ravensara oil	1944-1388	1
Taoasis	Ravensara oil	2427-5280	1
Taoasis	Ravensara oil	231012-118739	2

- 8580 spectra from 736 *Apo-Ident* customers from a total of 3531 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ravensara oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ravensara oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	160	0	20 641
Type C	0	20	0	8580

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.7880 %)	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 *Ravensara oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Hyssop oil	23.26	–
Sage oil	26.01	–
Citus oil	28.15	–
Rosemary camphor oil	34.24	–
Angelica root oil	35.92	–
Myrtle oil	40.47	–
Yarrow oil	41.98	–
Marjoram oil	42.23	–
Rosemary oil	42.49	–
Eucalyptus oil	45.03	–
Niaouli oil	45.27	–
Cajeput (essentiel oil)	46.38	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31635	31635	0.00	23.26
33872	33872	0.00	24.60
33854	33854	0.00	25.96

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 2.3-2021-01

Validated substance/substance group	**Rose-geranium oil, organic**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30536-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Rose-geranium oil, organic; Oleum pelargonium graveolens

Special notes

When selecting the *Rose-geranium oil, organic* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Rose-geranium oil, organic	3	2	25

Second-stage model

For differentiation of the substance/substance group *Rose-geranium oil, organic* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Rose-geranium oil, organic*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Rose-geranium oi…	21027-119997	31698	60	not required
Taoasis	Rose-geranium oi…	21027-121893	31776	60	not required
Taoasis	Rose-geranium oi…	21027-121893	31951	60	not required
Taoasis	Rose-geranium oi…	1616008-125056	33036	40	not required

Validation samples

A total of 53 906 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 *Rose-geranium oil, organic*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.

- 24 285 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Rose-geranium oil, organic*.

- 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
Primavera	Rose-geranium oil, organic	00492L26	34372	40
Taoasis	Rose-geranium oil, organic	2260-2430	34042	40
Taoasis	Rose-geranium oil, organic	1616008-125056	33037	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 25 batches from the substance/substance group *Rose-geranium oil, organic*.

- 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
Apomix	Rose-geranium oil, organic	2260-2431	1
Biofrid	Rose-geranium oil, organic	5010	1
Bombastus	Rose-geranium oil, organic	22625-106677	1
Primavera	Rose-geranium oil, organic	8304131	1
Primavera/Primavera	Rose-geranium oil, organic	618L23	1
Taoasis	Rose-geranium oil, organic	130111-112615	1
Taoasis	Rose-geranium oil, organic	130111-110467	1
Taoasis	Rose-geranium oil, organic	130729-113060	1
Taoasis	Rose-geranium oil, organic	401011-117641	1
Taoasis	Rose-geranium oil, organic	401011-117806	2
Taoasis	Rose-geranium oil, organic	21027-119121	1
Taoasis	Rose-geranium oil, organic	21027-121337	1
Taoasis	Rose-geranium oil, organic	1500969-123554	1
Taoasis	Rose-geranium oil, organic	21027-120292	1
Taoasis	Rose-geranium oil, organic	A1616008-128497	1
Taoasis	Rose-geranium oil, organic	1840-128860	2
Taoasis	Rose-geranium oil, organic	1840-374	2
Taoasis	Rose-geranium oil, organic	2445-3346	1
Taoasis	Rose-geranium oil, organic	2445-3947	3
Taoasis	Rose-geranium oil, organic	2445-6615	1
Taoasis/Taoasis	Rose-geranium oil, organic	22625-104463	1
Taoasis/Taoasis	Rose-geranium oil, organic	B1840-128497	1
Taoasis/Taoasis	Rose-geranium oil, organic	2260-2430	1
Taoasis/Taoasis	Rose-geranium oil, organic	2445-5861	1
Taoasis/Taoasis	Rose-geranium oil, organic	4502-9228	1

- 8570 spectra from 736 *Apo-Ident* customers from a total of 3521 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Rose-geranium oil, organic* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Rose-geranium oil, organic* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 285
Type B	0	120	0	20 681
Type C	0	30	0	8570

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.2727 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7869 %)	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 *Rose-geranium oil, organic* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citronella oil	24.66	–
alpha-bisabolol (racemic) at least 85%	33.51	–
Marjoram oil	49.88	–
Carrot seed oil	52.90	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31698	31698	0.00	33.18
31776	31776	0.00	34.23
31951	31951	0.00	33.89
33036	33036	0.00	27.78

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 2.3-2021-01

Validated substance/substance group	**Rosemary camphor oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33803-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Rosemary camphor oil

Special notes

When selecting the *Rosemary camphor oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Rosemary camphor oil	2	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Rosemary camphor oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Rosemary camphor…	00536K25	33803	40	not required
Primavera	Rosemary camphor…	00559B26	33959	40	not required

Validation samples

A total of 53 906 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 *Rosemary camphor oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Rosemary camphor oil*.
- 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
Primavera	Rosemary camphor oil	00179G26	34170	40
Primavera	Rosemary camphor oil	00631A27	34373	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Rosemary camphor oil*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Rosemary camphor oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Rosemary camphor oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	80	0	20 721
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Rosemary camphor oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rosemary oil	19.85	–
Eucalyptus oil	21.03	–
Citus oil	26.95	–
Hyssop oil	26.99	–
Niaouli oil	29.08	–
Ravensara oil	32.27	–
Cajeput (essentiel oil)	34.68	–
Sage oil	37.28	–
Myrtle oil	47.15	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33803	33803	0.00	20.26
33959	33959	0.00	19.85

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 2.3-2021-01

Validated substance/substance group	**Rosewood oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31556-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Rosewood oil; Oleum aniba roseodora

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Rosewood oil	3	2	16

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Rosewood oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Rosewood oil	11572-116545	31556	60	not required
Taoasis	Rosewood oil	4381004-120355	31688	60	not required
Taoasis	Rosewood oil	42543-2657	34106	40	not required

Validation samples

A total of 53 906 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 *Rosewood oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Rosewood oil*.
- 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
Primavera	Rosewood oil	00632H26	34381	40
Taoasis	Rosewood oil	5101015-124967	32801	40
Taoasis	Rosewood oil	5101015-124967	33048	40

- 20 681 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 3 *Apo-Ident* customers from 16 batches from the substance/substance group *Rosewood oil*.

- 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
Taoasis	Rosewood oil	4381004-1200355	1
Taoasis	Rosewood oil	4381004-121143	2
Taoasis	Rosewood oil	4381004-122041	2
Taoasis	Rosewood oil	5101017-122566	2
Taoasis	Rosewood oil	5101015-123299	1
Taoasis	Rosewood oil	5101015-124967	3
Taoasis	Rosewood oil	5101015-124243	1
Taoasis	Rosewood oil	42543-126343	1
Taoasis	Rosewood oil	42543-127664	1
Taoasis	Rosewood oil	42543-128666	1
Taoasis	Rosewood oil	42543-128055	2
Taoasis	Rosewood oil	42543-146	4
Taoasis	Rosewood oil	42543-2053	2
Taoasis	Rosewood oil	109177-5788	4
Taoasis	Rosewood oil	9177-3983	2
Taoasis GmbH/ Taoasis	Rosewood oil	109177-5788	1
Taoasis/Taoasis	Rosewood oil	109177-5863	1

- 8569 spectra from 736 *Apo-Ident* customers from a total of 3530 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Rosewood oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Rosewood oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	120	0	20 659
Type C	0	31	0	8569

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9458 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7869 %)	100.0000 % (> 80.6452 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Thyme oil, white	39.75	–
Coriander oil	59.34	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31556	31556	0.00	44.34
31688	31688	0.00	50.64
34106	34106	0.00	39.75

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

VALIDATION REPORT

IdentModule 2.3-2021-01

Validated substance/substance group	**Sage oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31139-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Sage oil; Oleum salviae

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Sage oil	3	1	12

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Sage oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Sage oil	526975-112642BAG90451	31139	40	not required
Taoasis	Sage oil	34052-114939	31257	40	not required
Taoasis	Sage oil	8461016-122272	31783	60	not required

Validation samples

A total of 53 906 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 *Sage oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Sage oil*.
- 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
Taoasis	Sage oil	8461016-126496	33034	40
Taoasis	Sage oil	8461016-126496	33035	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 4 *Apo-Ident* customers from 12 batches from the substance/substance group *Sage oil*.
- 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	Sage oil	309857	1
Bombastus	Sage oil	18004276	2
Taoasis	Sage oil	13988-117449	1
Taoasis	Sage oil	21190-119239	1
Taoasis	Sage oil	21190-118009	1
Taoasis	Sage oil	29944-120889	1
Taoasis	Sage oil	29944-120965	1
Taoasis	Sage oil	8461016-774	2
Taoasis	Sage oil	8461016-127221	1
Taoasis	Sage oil	8461016-3526	2
Taoasis	Sage oil	461016-6429	2
Taoasis	Sage oil	8461016-2158	1

- 8584 spectra from 736 *Apo-Ident* customers from a total of 3535 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Sage oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sage oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	80	0	20 721
Type C	0	14	2	8584

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7888 %)	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 *Sage oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Rosemary camphor oil	22.94	–
Eucalyptus oil	31.34	–
Matricaria oil, roman	35.10	–
Hyssop oil	36.28	–
Rosemary oil	38.79	–
Ravensara oil	38.93	–
Silver fir oil	45.21	–
Citus oil	53.35	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31257	31257	0.00	36.31
31783	31783	0.00	31.26
31139	31139	0.00	36.28

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 2.3-2021-01

Validated substance/substance group	**Salicylic white paraffin 10%**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31521-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Salicylic white paraffin 10%; Acidum salicylicum cum vaselino albo 10 %

Special notes

When selecting the *Salicylic white paraffin 10%* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

A sample is considered independent 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 white paraffin 10%	3	2	12

Second-stage model

For differentiation of the substance/substance group *Salicylic white paraffin 10%* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan 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 white paraffin 10%*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Bombastus	Salicylic white …	287820	31521	60	not required
Bombastus	Salicylic white …	291886	31629	75	not required
Bombastus	Salicylic white …	310227	33473	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 175 spectra of 3 reference samples from the substance/substance group *Salicylic white paraffin 10%*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 330 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Salicylic white paraffin 10%*.
- 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
Bombastus	Salicylic white paraffin 10%	302737	32741	40
Bombastus	Salicylic white paraffin 10%	309004	33416	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 10 *Apo-Ident* customers from 12 batches from the substance/substance group *Salicylic white paraffin 10%*.
- 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	Salicylic white paraffin 10%	19003777	1
Bombastus	Salicylic white paraffin 10%	17000464	1
Bombastus	Salicylic white paraffin 10%	293212	1
Caelo	Salicylic white paraffin 10%	19140601	1
Caelo	Salicylic white paraffin 10%	16120701	2
Caelo	Salicylic white paraffin 10%	15394702	1
Caelo	Salicylic white paraffin 10%	16214203	1
Caelo	Salicylic white paraffin 10%	16214202	1
Caelo	Salicylic white paraffin 10%	18114703	1
Caelo	Salicylic white paraffin 10%	18245603	1
Eigenrezeptur	Salicylic white paraffin 10%	150702	1
Winthrop Arzneimittel	Salicylic white paraffin 10%	IE6931	1

- 8587 spectra from 735 *Apo-Ident* customers from a total of 3534 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance 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 white paraffin 10%* can clearly be 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 white paraffin 10%* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	175	0	24 330
Type B	0	80	0	20 721
Type C	0	13	0	8587

The substance/substance group *Salicylic white paraffin 10%* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 96.5714 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7898 %)	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 *Salicylic white paraffin 10%* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* 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 ointment (stabilised)	46.25	–
Neribas® fat ointment	48.95	–
Cottonwood ointment	52.82	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Salicylic white paraffin 10%* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31629	31629	0.00	62.60
33473	33473	0.00	62.26
31521	31521	0.00	62.90

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 2.3-2021-01

Validated substance/substance group	**Salmon oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33088-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Salmon oil

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Salmon oil	2	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Salmon oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Salmon oil	170345	33088	40	20170213*
Caelo	Salmon oil	173079	34225	40	20171116*

Validation samples

A total of 53 906 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 *Salmon oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Salmon oil*.
- 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	Salmon oil	182524	34341	40
Caelo	Salmon oil	20000795	35034	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Salmon oil*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Salmon oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Salmon oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	80	0	20 721
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Salmon oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Argan oil	47.95	–
Balm Bio Nature	53.78	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33088	33088	0.00	44.96
34225	34225	0.00	50.92

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 2.3-2021-01

Validated substance/substance group	**Sandalwood oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33799-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Sandalwood oil

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Sandalwood oil	3	3	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Sandalwood oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Sandalwood oil	00891G25	33799	40	not required
Primavera	Sandalwood oil	00141L25	33801	40	not required
Taoasis	Sandalwood oil	145-505	33832	40	not required

Validation samples

A total of 53 906 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 *Sandalwood oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 385 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Sandalwood oil*.
- 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
Primavera	Sandalwood oil	00474C26	34173	40
Primavera	Sandalwood oil	00346L26	34408	40
Taoasis	Sandalwood oil	128319	33833	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Sandalwood oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Sandalwood oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Sandalwood oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	120	0	20 681
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Sandalwood oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Savory herb	114.91	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33799	33799	0.00	131.96
33832	33832	0.00	132.91
33801	33801	0.00	141.68

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 2.3-2021-01

Validated substance/substance group	**Savory herb**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33820-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Savory herb

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Savory herb	2	1	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Savory herb*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Savory herb	498	33820	40	not required
Taoasis	Savory herb	1569-129318	33821	40	not required

Validation samples

A total of 53 906 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 *Savory herb*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Savory herb*.
- 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
Taoasis	Savory herb	1742-3729	34281	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Savory herb*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Savory herb* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Savory herb* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	40	0	20 761
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Savory herb* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Thyme oil, red	24.09	–
Oregano oil	41.03	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33820	33820	0.00	26.50
33821	33821	0.00	24.09

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 2.3-2021-01

Validated substance/substance group	**Sebexol® formula basis / Sebexol® cream lotion / Wofacutan w**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30839-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver; Hans Karrer Hydrocream MicroSilver; Sebexol® basic pH 5 formula basis; Sebexol® cream lotion pH 5; Wofacutan wash lotion

Special notes

When selecting the *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Hans Karrer Hydrocream MicroSilver	3	2	7
Sebexol® basic pH 5 formula basis	3	2	55
Sebexol® cream lotion pH 5	5	1	92
Wofacutan wash lotion	3	1	9

Second-stage model

For differentiation of the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Hans Karrer G...	Hans Karrer Hydr...	16001	33190	40	not required
Hans Karrer G...	Hans Karrer Hydr...	16002	33191	40	not required
Hans Karrer G...	Hans Karrer Hydr...	18002	34116	40	not required
Devesa	Sebexol® basic p...	1307	31104	40	1403098
Devesa	Sebexol® basic p...	1522	31961	60	not required
Devesa	Sebexol® basic p...	1638124	32744	40	not required
Devesa	Sebexol® cream l...	1220	30839	40	1403097
Devesa	Sebexol® cream l...	1317	31103	40	not required
Devesa	Sebexol® cream l...	1412	31592	45	not required
Devesa	Sebexol® cream l...	1531	31839	60	not required
Devesa	Sebexol® cream l...	1552.2	32743	40	not required
Kesla Pharma	Wofacutan wash l...	0974.12	30972	80	not required
Kesla Pharma	Wofacutan wash l...	0389.13	31065	40	not required
Kesla Pharma	Wofacutan wash l...	0868.16	33483	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 645 spectra of 14 reference samples from the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver*. These samples are listed above in the *calibration samples* section. The reference samples come from 14 different batches.

- 23 860 spectra from a total of 491 batches from further 157 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied

Type B spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver.*
- 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
Hans Karrer GmbH	Hans Karrer Hydrocream Micro…	16003	33192	40
Hans Karrer GmbH	Hans Karrer Hydrocream Micro…	16004	33193	40
Devesa	Sebexol® basic pH 5 formula …	1712122	33427	40
Devesa	Sebexol® basic pH 5 formula …	1644102	33432	40
Devesa	Sebexol® cream lotion pH 5	1605101	32907	40
Kesla Pharma	Wofacutan wash lotion	0729.16	32913	40
Devesa	Sebexol® cream lotion pH 5	1605101	32908	40
Kesla Pharma	Wofacutan wash lotion	0729.16	32914	40

- 20 481 spectra from a total of 441 batches from further 200 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 764 spectra from 121 *Apo-Ident* customers from 162 batches from the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver.*
- Among them are spectra of independent samples from 135 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

Supplier	Substance	Batch	Spectra
Hans Karrer / Anzag	Hans Karrer Hydrocream Micro…	18002	1
Hans Karrer GmbH /107	Hans Karrer Hydrocream Micro…	LOT19001	1
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	18001	1
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	18003	4
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	18004	1
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	19001	5
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	20001	1
Hans Karrer/Phönix	Hans Karrer Hydrocream Micro…	19003	3
hanskarrer / Gehe	Hans Karrer Hydrocream Micro…	18001	1
Hanskarrer / Gehe	Hans Karrer Hydrocream Micro…	18002	1
Hanskarrer / Gehe	Hans Karrer Hydrocream Micro…	18003	1
Hanskarrer / Gehe	Hans Karrer Hydrocream Micro…	18004	1
Hans-Karrer GmbH	Hans Karrer Hydrocream Micro…	18003	1
HansKarrer/Krieger	Hans Karrer Hydrocream Micro…	19003	1
Bombastus	Sebexol® basic pH 5 formula …	1346	2

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Supplier	Substance	Batch	Spectra
Caelo	Sebexol® basic pH 5 formula ...	1440	1
Caelo	Sebexol® basic pH 5 formula ...	1604127	2
Caelo	Sebexol® basic pH 5 formula ...	1239	1
Caelo	Sebexol® basic pH 5 formula ...	1131	2
Caelo	Sebexol® basic pH 5 formula ...	1620117	2
Caelo	Sebexol® basic pH 5 formula ...	1851119	2
Caelo	Sebexol® basic pH 5 formula ...	1817126	1
devesa	Sebexol® basic pH 5 formula ...	1719111	3
Devesa	Sebexol® basic pH 5 formula ...	I307	1
Devesa	Sebexol® basic pH 5 formula ...	I232	1
Devesa	Sebexol® basic pH 5 formula ...	1232	1
Devesa	Sebexol® basic pH 5 formula ...	1239	1
Devesa	Sebexol® basic pH 5 formula ...	1328	5
Devesa	Sebexol® basic pH 5 formula ...	1335	2
Devesa	Sebexol® basic pH 5 formula ...	1404	1
Devesa	Sebexol® basic pH 5 formula ...	1407	2
Devesa	Sebexol® basic pH 5 formula ...	1430	1
Devesa	Sebexol® basic pH 5 formula ...	1511	2
Devesa	Sebexol® basic pH 5 formula ...	1440	4
Devesa	Sebexol® basic pH 5 formula ...	1543	5
Devesa	Sebexol® basic pH 5 formula ...	1604127	4
Devesa	Sebexol® basic pH 5 formula ...	1620117	1
Devesa	Sebexol® basic pH 5 formula ...	1683124	1
Devesa	Sebexol® basic pH 5 formula ...	1644102	3
Devesa	Sebexol® basic pH 5 formula ...	1712122	3
Devesa	Sebexol® basic pH 5 formula ...	1719111	3
Devesa	Sebexol® basic pH 5 formula ...	1807113	2
Devesa	Sebexol® basic pH 5 formula ...	1828110	2
Devesa	Sebexol® basic pH 5 formula ...	1851119	2
Devesa	Sebexol® basic pH 5 formula ...	1912118	2
Devesa	Sebexol® basic pH 5 formula ...	1923107	2
Devesa	Sebexol® basic pH 5 formula ...	1946114	1
DEVESA	Sebexol® basic pH 5 formula ...	1318	2
DEVESA	Sebexol® basic pH 5 formula ...	1328	2
DEVESA	Sebexol® basic pH 5 formula ...	1440	2
DEVESA	Sebexol® basic pH 5 formula ...	1511	1
DEVESA	Sebexol® basic pH 5 formula ...	1644102	1
DEVESA	Sebexol® basic pH 5 formula ...	1712122	1
DEVESA	Sebexol® basic pH 5 formula ...	1719111	1
DEVESA	Sebexol® basic pH 5 formula ...	1807113	3
DEVESA	Sebexol® basic pH 5 formula ...	1817126	1
DEVESA	Sebexol® basic pH 5 formula ...	185119	1
DEVESA	Sebexol® basic pH 5 formula ...	1923107	1
DEVESA	Sebexol® basic pH 5 formula ...	1912118	1
DEVESA	Sebexol® basic pH 5 formula ...	1935126	1
Devesa / Gehe	Sebexol® basic pH 5 formula ...	1817126	1
Devesa / Kehr	Sebexol® basic pH 5 formula ...	1644102	1
Devesa / Noweda	Sebexol® basic pH 5 formula ...	1620117	1
Devesa / Noweda	Sebexol® basic pH 5 formula ...	1638124	1
Devesa / Noweda	Sebexol® basic pH 5 formula ...	170420S/1620117	1
Devesa / Noweda	Sebexol® basic pH 5 formula ...	170516S/1644102	1
DEVESA / Noweda	Sebexol® basic pH 5 formula ...	1712122	3
DEVESA /G	Sebexol® basic pH 5 formula ...	1912118	1
Devesa Dr.Reingraber GmbH	Sebexol® basic pH 5 formula ...	1425	1
DEVESA Dr.Reingraber GmbH	Sebexol® basic pH 5 formula ...	1328	1
Devesa Dr.Reingraber Gm...	Sebexol® basic pH 5 formula ...	1244	1
Devesa Dr.Reingraber Gm...	Sebexol® basic pH 5 formula ...	1303	1
Devesa- Phönix	Sebexol® basic pH 5 formula ...	1604127	1
Devesa/ Noweda	Sebexol® basic pH 5 formula ...	1712122	1
Devesa/ Ebert	Sebexol® basic pH 5 formula ...	1817126	1

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Supplier	Substance	Batch	Spectra
Devesa/ Fiebig	Sebexol® basic pH 5 formula ...	1338	1
Devesa/ Phoenix	Sebexol® basic pH 5 formula ...	1543	1
Devesa/AHD	Sebexol® basic pH 5 formula ...	1245	4
Devesa/AHD	Sebexol® basic pH 5 formula ...	1328	7
Devesa/Alliance	Sebexol® basic pH 5 formula ...	2009126	2
Devesa/Alliance	Sebexol® basic pH 5 formula ...	1946114	2
devesa/gehe	Sebexol® basic pH 5 formula ...	1346	1
devesa/gehe	Sebexol® basic pH 5 formula ...	1356	1
Devesa/Gehe	Sebexol® basic pH 5 formula ...	1851119	1
Devesa/Gehe	Sebexol® basic pH 5 formula ...	1912118	1
Devesa/Gehe	Sebexol® basic pH 5 formula ...	1923107	2
Devesa/Gehe	Sebexol® basic pH 5 formula ...	1935126	2
Devesa/Gehe	Sebexol® basic pH 5 formula ...	1946114	1
Devesa/Kehr	Sebexol® basic pH 5 formula ...	1407	2
Devesa/Kehr	Sebexol® basic pH 5 formula ...	1620117	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1430	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1440	2
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1638124	2
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1604127	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1719111/05	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1807113	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1828110	1
Devesa/Noweda	Sebexol® basic pH 5 formula ...	1946114	2
DEVESA/Noweda	Sebexol® basic pH 5 formula ...	1604127	1
DEVESA/Noweda	Sebexol® basic pH 5 formula ...	1543	1
Devesa/Phönix	Sebexol® basic pH 5 formula ...	1543	3
Devesa/Phönix	Sebexol® basic pH 5 formula ...	1620117	2
Devesa/Phönix	Sebexol® basic pH 5 formula ...	1712122	2
Devesa/Phönix	Sebexol® basic pH 5 formula ...	2031128	2
DEVESA/Phönix	Sebexol® basic pH 5 formula ...	1851119	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1440	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1522	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1543	4
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1620117	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1638124	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1644102	2
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1712122	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1719111	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1807113	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1817126	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1746116	2
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	187126/06	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1828110	2
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1851119	1
Devesa/Sanacorp	Sebexol® basic pH 5 formula ...	1935126	1
Dr Reinhard GmbH- Kehr	Sebexol® basic pH 5 formula ...	1620117	1
Dr. Reingraber GmbH	Sebexol® basic pH 5 formula ...	1708120	1
Dr.Reingraber GmbH	Sebexol® basic pH 5 formula ...	1232	1
Dr.Reingraber/sanacorp	Sebexol® basic pH 5 formula ...	1719111	1
Dr.Reingraber/sanacorp	Sebexol® basic pH 5 formula ...	1923107	1
Eigenherstellung	Sebexol® basic pH 5 formula ...	1328	1
Fagron	Sebexol® basic pH 5 formula ...	1425	1
Fagron	Sebexol® basic pH 5 formula ...	1510	2
Fiebig	Sebexol® basic pH 5 formula ...	1511	2
Gehe	Sebexol® basic pH 5 formula ...	1935126	2
Holdermann	Sebexol® basic pH 5 formula ...	1307	1
Ichthyol	Sebexol® basic pH 5 formula ...	1232	2
Kehr/ Devesa	Sebexol® basic pH 5 formula ...	1644102	1
Kehr/ Devesa	Sebexol® basic pH 5 formula ...	1746116	4
Kehr/Devesa	Sebexol® basic pH 5 formula ...	1817126	2

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Supplier	Substance	Batch	Spectra
Kehr/Devesa	Sebexol® basic pH 5 formula ...	1828110	2
noweda	Sebexol® basic pH 5 formula ...	2009126	1
Noweda	Sebexol® basic pH 5 formula ...	1328	1
Noweda / Dewesa	Sebexol® basic pH 5 formula ...	1719111	1
Noweda /Devesa	Sebexol® basic pH 5 formula ...	1644102	3
Noweda/Devesa	Sebexol® basic pH 5 formula ...	2x1407	1
Phoenix	Sebexol® basic pH 5 formula ...	1440	1
Phoenix/Devesa	Sebexol® basic pH 5 formula ...	1215	1
Phoenix/Devesa	Sebexol® basic pH 5 formula ...	1407	1
Phoenix/Devesa	Sebexol® basic pH 5 formula ...	1604127	1
Phönix	Sebexol® basic pH 5 formula ...	1313	2
Phönix	Sebexol® basic pH 5 formula ...	1416	1
Phönix	Sebexol® basic pH 5 formula ...	1425	2
Phönix / Devesa	Sebexol® basic pH 5 formula ...	1644102	1
Sanacorp	Sebexol® basic pH 5 formula ...	1313	1
Sebexol	Sebexol® basic pH 5 formula ...	1313	1
Sebexol	Sebexol® basic pH 5 formula ...	1333	1
Sebexol/ Noweda	Sebexol® basic pH 5 formula ...	1403	1
Sebexol/ Noweda	Sebexol® basic pH 5 formula ...	1430	1
Sebexol/AHD	Sebexol® basic pH 5 formula ...	1303	2
Astellas	Sebexol® cream lotion pH 5	1504	2
Caelo	Sebexol® cream lotion pH 5	1511	2
Caelo	Sebexol® cream lotion pH 5	1417	1
Caelo	Sebexol® cream lotion pH 5	1504	1
Caelo	Sebexol® cream lotion pH 5	4117E-03872	1
Caelo	Sebexol® cream lotion pH 5	1604129	1
Caelo	Sebexol® cream lotion pH 5	1605101	3
Caelo	Sebexol® cream lotion pH 5	1727207	1
Caelo	Sebexol® cream lotion pH 5	1807113	2
Caelo	Sebexol® cream lotion pH 5	1812123	2
Caelo	Sebexol® cream lotion pH 5	1828110	1
Caelo	Sebexol® cream lotion pH 5	1531	1
Caelo	Sebexol® cream lotion pH 5	1912119	1
Caelo	Sebexol® cream lotion pH 5	1736105	3
deversa	Sebexol® cream lotion pH 5	1935227	5
Deversa/Fiebig	Sebexol® cream lotion pH 5	1817127	1
Deversa/Fiebig	Sebexol® cream lotion pH 5	1824115	1
devesa	Sebexol® cream lotion pH 5	1746116	1
Devesa	Sebexol® cream lotion pH 5	1510	4
Devesa	Sebexol® cream lotion pH 5	1523	3
Devesa	Sebexol® cream lotion pH 5	1524	1
Devesa	Sebexol® cream lotion pH 5	1604128	1
Devesa	Sebexol® cream lotion pH 5	1708120	3
Devesa	Sebexol® cream lotion pH 5	1417N-03872	1
Devesa	Sebexol® cream lotion pH 5	1651121	2
Devesa	Sebexol® cream lotion pH 5	1727107	1
Devesa	Sebexol® cream lotion pH 5	1736106	1
Devesa	Sebexol® cream lotion pH 5	1746116	4
Devesa	Sebexol® cream lotion pH 5	1743225	1
Devesa	Sebexol® cream lotion pH 5	1802108/01	1
Devesa	Sebexol® cream lotion pH 5	1817127	2
Devesa	Sebexol® cream lotion pH 5	1604328	1
Devesa	Sebexol® cream lotion pH 5	1812223	5
Devesa	Sebexol® cream lotion pH 5	1817227	1
Devesa	Sebexol® cream lotion pH 5	1824115	3
Devesa	Sebexol® cream lotion pH 5	1901102	3
Devesa	Sebexol® cream lotion pH 5	1901103	1
Devesa	Sebexol® cream lotion pH 5	1912119	1
Devesa	Sebexol® cream lotion pH 5	1912120	2
Devesa	Sebexol® cream lotion pH 5	1923108	1

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Supplier	Substance	Batch	Spectra
Devesa	Sebexol® cream lotion pH 5	1935127	2
Devesa	Sebexol® cream lotion pH 5	1923108/06-2022	1
Devesa	Sebexol® cream lotion pH 5	1925121	1
Devesa	Sebexol® cream lotion pH 5	1939227	1
Devesa	Sebexol® cream lotion pH 5	1947118	1
Devesa	Sebexol® cream lotion pH 5	2004120	2
DEVESA	Sebexol® cream lotion pH 5	1505	1
DEVESA	Sebexol® cream lotion pH 5	1510	1
DEVESA	Sebexol® cream lotion pH 5	1523	1
DEVESA	Sebexol® cream lotion pH 5	1531	1
DEVESA	Sebexol® cream lotion pH 5	1651120	2
DEVESA	Sebexol® cream lotion pH 5	1708120	1
DEVESA	Sebexol® cream lotion pH 5	1736105	1
DEVESA	Sebexol® cream lotion pH 5	1802108/01	1
DEVESA	Sebexol® cream lotion pH 5	1743225	1
DEVESA	Sebexol® cream lotion pH 5	1812123	2
DEVESA	Sebexol® cream lotion pH 5	1817227	1
DEVESA	Sebexol® cream lotion pH 5	1824215	1
DEVESA	Sebexol® cream lotion pH 5	1836106	2
DEVESA	Sebexol® cream lotion pH 5	1912120	1
DEVESA	Sebexol® cream lotion pH 5	1901103	1
DEVESA	Sebexol® cream lotion pH 5	1939227	2
Devesa /	Sebexol® cream lotion pH 5	1511	1
Devesa /	Sebexol® cream lotion pH 5	1812223	1
Devesa /	Sebexol® cream lotion pH 5	1912119	1
Devesa /	Sebexol® cream lotion pH 5	1923108	2
DEVESA / Anzag	Sebexol® cream lotion pH 5	1605101	1
DEVESA / Anzag	Sebexol® cream lotion pH 5	1802208	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1736106	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1743125	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1746116	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1802208	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1812123	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1828110	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1912120	1
devesa / Fiebig	Sebexol® cream lotion pH 5	1935227	1
Devesa / Gehe	Sebexol® cream lotion pH 5	1517	1
Devesa / Gehe	Sebexol® cream lotion pH 5	1530	2
Devesa / Gehe	Sebexol® cream lotion pH 5	1651120	1
Devesa / Gehe	Sebexol® cream lotion pH 5	1727107	1
Devesa / Gehe	Sebexol® cream lotion pH 5	1736106	2
Devesa / Gehe	Sebexol® cream lotion pH 5	1746116	3
Devesa / Gehe	Sebexol® cream lotion pH 5	1824215	2
Devesa / Gehe	Sebexol® cream lotion pH 5	1923108	1
Devesa / Gehe	Sebexol® cream lotion pH 5	1935127	1
Devesa / Gehe 08.12.18	Sebexol® cream lotion pH 5	1824215-S20190115Ma7	1
Devesa / Gehe 15.3.18	Sebexol® cream lotion pH 5	1743225-20180404Ma10	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1430	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1531	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1644102	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1712223	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1736106	2
Devesa / Noweda	Sebexol® cream lotion pH 5	1720115	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1802208	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1807113	1
Devesa / Noweda	Sebexol® cream lotion pH 5	1836105	3
Devesa / Noweda	Sebexol® cream lotion pH 5	1912119	1
Devesa / Phönix	Sebexol® cream lotion pH 5	1812123	1
Devesa / Sanacorp	Sebexol® cream lotion pH 5	1828111	2
Devesa /Gehe	Sebexol® cream lotion pH 5	1901103	1

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Supplier	Substance	Batch	Spectra
Devesa /Phönix	Sebexol® cream lotion pH 5	1807113	9
Devesa Dr.Reingraben/Sa...	Sebexol® cream lotion pH 5	1743125	1
Devesa Dr.Reingraben/Sa...	Sebexol® cream lotion pH 5	1817127	3
Devesa Dr.Reingraber GmbH	Sebexol® cream lotion pH 5	1935127	1
Devesa Dr.Reingraber GmbH	Sebexol® cream lotion pH 5	2009227	1
Devesa Dr.Reingraber/Sa...	Sebexol® cream lotion pH 5	1925121	1
Devesa Dr.Reingraber/Sa...	Sebexol® cream lotion pH 5	1939127	3
Devesa GmbH /Alliance H...	Sebexol® cream lotion pH 5	1712223	1
Devesa GmbH /Alliance H...	Sebexol® cream lotion pH 5	1828111	1
Devesa GmbH /Alliance H...	Sebexol® cream lotion pH 5	1828110	1
devesa Noweda	Sebexol® cream lotion pH 5	1802208	1
devesa phoenix	Sebexol® cream lotion pH 5	1925121	1
devesa phoenix	Sebexol® cream lotion pH 5	1947119	1
devesa phoenix	Sebexol® cream lotion pH 5	2009227	2
Devesa/	Sebexol® cream lotion pH 5	1504	2
Devesa/	Sebexol® cream lotion pH 5	1524	1
Devesa/	Sebexol® cream lotion pH 5	1604129	4
Devesa/	Sebexol® cream lotion pH 5	1644102	1
Devesa/	Sebexol® cream lotion pH 5	17433225	1
Devesa/	Sebexol® cream lotion pH 5	1947118	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1817227	1
Devesa/ Fiebig	Sebexol® cream lotion pH 5	1712223	2
Devesa/ Fiebig	Sebexol® cream lotion pH 5	1935227	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1736105	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1802208	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1807113	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1935227	2
Devesa/ Noweda	Sebexol® cream lotion pH 5	1901103	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1939227	4
Devesa/ Noweda	Sebexol® cream lotion pH 5	1947118	1
Devesa/ Noweda	Sebexol® cream lotion pH 5	1947119	2
Devesa/ Phoenix	Sebexol® cream lotion pH 5	1620117	1
Devesa/ Phoenix	Sebexol® cream lotion pH 5	1817127	1
DEVESA/ Phoenix	Sebexol® cream lotion pH 5	1939127/09	1
Devesa/ Phönix	Sebexol® cream lotion pH 5	1524	1
Devesa/ Phönix	Sebexol® cream lotion pH 5	1727207	1
Devesa/ Phönix	Sebexol® cream lotion pH 5	1736105	2
Devesa/ Phönix	Sebexol® cream lotion pH 5	1736106	6
Devesa/ Phönix	Sebexol® cream lotion pH 5	1743225	2
Devesa/ Phönix	Sebexol® cream lotion pH 5	1812223	3
Devesa/ Sanacorp	Sebexol® cream lotion pH 5	1925121	1
Devesa/ Sanacorp	Sebexol® cream lotion pH 5	1923108	1
Devesa/ Sanacorp	Sebexol® cream lotion pH 5	1912120	1
Devesa/ Sanacorp	Sebexol® cream lotion pH 5	1939127	1
Devesa/ Sanacorp	Sebexol® cream lotion pH 5	20042120	1
Devesa/Fiebig	Sebexol® cream lotion pH 5	1426	1
Devesa/Fiebig	Sebexol® cream lotion pH 5	1712123	2
Devesa/Fiebig	Sebexol® cream lotion pH 5	1736105	5
Devesa/Fiebig	Sebexol® cream lotion pH 5	1824115	2
DEVESA/Fiebig	Sebexol® cream lotion pH 5	1925121	1
DEVESA/Fiebig	Sebexol® cream lotion pH 5	1935127	1
DEVESA/Fiebig	Sebexol® cream lotion pH 5	1947118	1
DEVESA/Fiebig	Sebexol® cream lotion pH 5	1939227	1
DEVESA/Fiebig	Sebexol® cream lotion pH 5	1947119	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1504	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1712123	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1644102	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1651121	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1817227	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1828111	1

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Supplier	Substance	Batch	Spectra
Devesa/Gehe	Sebexol® cream lotion pH 5	1836106	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1912119	1
Devesa/Gehe	Sebexol® cream lotion pH 5	1939127	1
Devesa/Kehr/25.05.2020	Sebexol® cream lotion pH 5	2004120	2
Devesa/NOW	Sebexol® cream lotion pH 5	1504/01	1
Devesa/NOW	Sebexol® cream lotion pH 5	1504	2
Devesa/NOW	Sebexol® cream lotion pH 5	1523	1
Devesa/NOW	Sebexol® cream lotion pH 5	1552	1
Devesa/NOW	Sebexol® cream lotion pH 5	1604228	1
Devesa/NOW	Sebexol® cream lotion pH 5	1604129	1
Devesa/NOW	Sebexol® cream lotion pH 5	1644102	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1447	3
Devesa/Noweda	Sebexol® cream lotion pH 5	1543	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1604228	5
Devesa/Noweda	Sebexol® cream lotion pH 5	1604328	5
Devesa/Noweda	Sebexol® cream lotion pH 5	1605201	3
Devesa/Noweda	Sebexol® cream lotion pH 5	1651121	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1651120	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1712123	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1719112	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1736105	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1736106	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1720115	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1743225	1
Devesa/Noweda	Sebexol® cream lotion pH 5	1935127	2
Devesa/Noweda	Sebexol® cream lotion pH 5	1947119	3
DEVESA/Noweda	Sebexol® cream lotion pH 5	1605201	2
Devesa/Phoenix	Sebexol® cream lotion pH 5	1511	1
devesa/Phönix	Sebexol® cream lotion pH 5	1727107	1
devesa/Phönix	Sebexol® cream lotion pH 5	1743125	5
devesa/Phönix	Sebexol® cream lotion pH 5	1746116	8
devesa/Phönix	Sebexol® cream lotion pH 5	1802208	5
devesa/Phönix	Sebexol® cream lotion pH 5	1824215	2
devesa/Phönix	Sebexol® cream lotion pH 5	18201402	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1708120	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1727207	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1817227	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1807113	2
Devesa/Phönix	Sebexol® cream lotion pH 5	1824215	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1828111	19
Devesa/Phönix	Sebexol® cream lotion pH 5	1901102	2
Devesa/Phönix	Sebexol® cream lotion pH 5	1901103	6
Devesa/Phönix	Sebexol® cream lotion pH 5	1912120	3
Devesa/Phönix	Sebexol® cream lotion pH 5	1923108	8
Devesa/Phönix	Sebexol® cream lotion pH 5	1925121	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1935227	6
Devesa/Phönix	Sebexol® cream lotion pH 5	1939127	5
Devesa/Phönix	Sebexol® cream lotion pH 5	1836105	1
Devesa/Phönix	Sebexol® cream lotion pH 5	1807113/02	1
Devesa/Phönix	Sebexol® cream lotion pH 5	2004120	1
Devesa/Phönix	Sebexol® cream lotion pH 5	2009227	1
DEVESA/Phönix	Sebexol® cream lotion pH 5	185119	1
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1511	1
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1530	2
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1743125	1
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1802108	1
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1828111	2
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1925121	2
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1901102	2
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1912120	1

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Supplier	Substance	Batch	Spectra
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1935127	1
Devesa/Sanacorp	Sebexol® cream lotion pH 5	1817127	1
Devesa/Sanacorp WE: 09....	Sebexol® cream lotion pH 5	1651121	1
Devesa-Fa.Gehe	Sebexol® cream lotion pH 5	1727207/-20180112Ma9	1
Devesa-Fa.Gehe	Sebexol® cream lotion pH 5	1824215-S20181115Ma2	1
Devesea	Sebexol® cream lotion pH 5	1604128	1
Divesa	Sebexol® cream lotion pH 5	1812223	1
Dr. Reingraber GmbH	Sebexol® cream lotion pH 5	1605103	1
Dr. Reingraber GmbH / F...	Sebexol® cream lotion pH 5	1824115	1
Euro OTC	Sebexol® cream lotion pH 5	1727207	1
Fagron	Sebexol® cream lotion pH 5	1517	1
Fiebig	Sebexol® cream lotion pH 5	1605101	2
Fiebig	Sebexol® cream lotion pH 5	1802108	1
Fiebig	Sebexol® cream lotion pH 5	1812223	1
Fiebig	Sebexol® cream lotion pH 5	1828111	1
Fiebig	Sebexol® cream lotion pH 5	1912119	1
Fiebig	Sebexol® cream lotion pH 5	1912120	1
Fiebig/Devesa	Sebexol® cream lotion pH 5	1817227	1
Fiebig/Devesa	Sebexol® cream lotion pH 5	1836105	2
Fiebig/Devesa	Sebexol® cream lotion pH 5	1912120	1
FIEBIG; HERSTELLER DEVE...	Sebexol® cream lotion pH 5	2004120	1
Gehe	Sebexol® cream lotion pH 5	1605103	1
Gehe	Sebexol® cream lotion pH 5	1727107	1
Geibo/Devesa	Sebexol® cream lotion pH 5	1947118	1
Hedinger/Noweda	Sebexol® cream lotion pH 5	18424115	1
Kehr 14.08.2020	Sebexol® cream lotion pH 5	2009227	1
Noweda	Sebexol® cream lotion pH 5	1651120	1
Noweda	Sebexol® cream lotion pH 5	1708120	1
Noweda	Sebexol® cream lotion pH 5	1712223	1
Noweda	Sebexol® cream lotion pH 5	1802108	1
Noweda	Sebexol® cream lotion pH 5	1817227	1
Noweda	Sebexol® cream lotion pH 5	1828111	1
Noweda	Sebexol® cream lotion pH 5	1836105	2
Noweda	Sebexol® cream lotion pH 5	1901103	1
Noweda	Sebexol® cream lotion pH 5	1901102	1
Noweda	Sebexol® cream lotion pH 5	1912119	1
Noweda	Sebexol® cream lotion pH 5	1925121	2
Noweda	Sebexol® cream lotion pH 5	1912120	1
Noweda	Sebexol® cream lotion pH 5	1923108	1
Noweda	Sebexol® cream lotion pH 5	1947118	1
Noweda	Sebexol® cream lotion pH 5	1947119	3
Noweda	Sebexol® cream lotion pH 5	2004120	1
Noweda	Sebexol® cream lotion pH 5	2019107	1
Noweda	Sebexol® cream lotion pH 5	2019207	1
Caelo	Sebexol® cream lotion pH 5	1712223	1
Caelo	Sebexol® cream lotion pH 5	1708120	3
Caelo	Sebexol® cream lotion pH 5	1719112	1
Noweda/devesa	Sebexol® cream lotion pH 5	1836106	1
Noweda/devesa	Sebexol® cream lotion pH 5	1923108	1
Noweda/devesa	Sebexol® cream lotion pH 5	1925121	1
Noweda/devesa	Sebexol® cream lotion pH 5	1947118	3
Noweda/Devesa	Sebexol® cream lotion pH 5	1638124	1
Phoenix/Devesa	Sebexol® cream lotion pH 5	1736105	1
Phoenix/Devesa	Sebexol® cream lotion pH 5	1812123	1
Phönix	Sebexol® cream lotion pH 5	160422	1
Phönix	Sebexol® cream lotion pH 5	1604129	1
Phönix	Sebexol® cream lotion pH 5	4217A-03872	1
Phönix	Sebexol® cream lotion pH 5	1828111	2
Phönix	Sebexol® cream lotion pH 5	1912120	1
Phönix/Devesa	Sebexol® cream lotion pH 5	1712123	1

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Supplier	Substance	Batch	Spectra
Phönix/Devesa	Sebexol® cream lotion pH 5	1651121	1
Phönix/Devesa	Sebexol® cream lotion pH 5	1824115	3
Phönix/Devesa	Sebexol® cream lotion pH 5	1817227	2
Phönix/Devesa	Sebexol® cream lotion pH 5	182811	1
Phönix/DEVESA	Sebexol® cream lotion pH 5	1935127	1
Römerapo.	Sebexol® cream lotion pH 5	1828110	1
Rondell Apotheke	Sebexol® cream lotion pH 5	1523	1
Sana/Devesa	Sebexol® cream lotion pH 5	1935127	1
Caelo	Sebexol® cream lotion pH 5	1430	1
Sanacorp / Devesa	Sebexol® cream lotion pH 5	1836106	1
sanacorp, 27.9.16,4,312EUR	Sebexol® cream lotion pH 5	1604328	1
Sebexol	Sebexol® cream lotion pH 5	1812123	1
Taosis	Sebexol® cream lotion pH 5	1828110	1
THC Pharma	Sebexol® cream lotion pH 5	1727107	1
Kesla Pharma/Phönix	Wofacutan wash lotion	58118	1
Kesla Pharma/Phönix	Wofacutan wash lotion	23819	2
Phönix Gotha	Wofacutan wash lotion	97913	1
Devesa	Sebexol® basic pH 5 formula ...	1307	5
Devesa	Sebexol® basic pH 5 formula ...		7
Devesa	Sebexol® basic pH 5 formula ...	1522	3
Devesa	Sebexol® basic pH 5 formula ...	1638124	2
Devesa/Gehe	Sebexol® basic pH 5 formula ...		1
Caelo	Sebexol® cream lotion pH 5		2
Devesa / Gehe	Sebexol® cream lotion pH 5		1
Devesa/	Sebexol® cream lotion pH 5		2
Devesa/fiebig	Sebexol® cream lotion pH 5		1
Devesa/NOW	Sebexol® cream lotion pH 5		1
Devesa/Noweda	Sebexol® cream lotion pH 5		1
Dr. Wolff	Sebexol® cream lotion pH 5		1
Gehe/Devesa	Sebexol® cream lotion pH 5		1
NOWEDA / HERSTELLER: DE...	Sebexol® cream lotion pH 5		1
Kesla Pharma/Noweda	Wofacutan wash lotion		2
Kesla/Noweda	Wofacutan wash lotion		5

- 7836 spectra from 731 *Apo-Ident* customers from a total of 3384 batches from a further 146 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	645	0	23 860
Type B	0	320	0	20 481
Type C	0	756	8	7836

The substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* can be clearly distinguished from all other substances.

In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9600 %)	100.0000 % (> 99.0698 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 98.7849 %)	98.9529 % (> 98.5602 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Excipial® U Hydrolotio	15.16	–
Fenistil® Gel	23.92	–
Dimeticone ointment 10% SR	26.38	–
Amciderm® Base cream	35.08	–
Linola® Sept	35.42	–
SyrSpend® SF pH4 cherry aroma	36.13	–
Abitima® clinic face cream	37.81	–
Aloe vera gel, 10x concentrated	42.26	–
Retterspitz external	42.76	–
SyrSpend® SF pH4 aroma free	43.39	–
Base cream Taoasis	43.68	–
Water	48.35	–
Bepanthen® solution	50.77	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sebexol® formula basis / Sebexol® cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30972	30972	0.00	21.64
31065	31065	0.00	23.18
33483	33483	0.00	23.12
33190	33190	0.00	23.62
33191	33191	0.00	22.06
34116	34116	0.00	20.54
32744	32744	0.00	16.95
31104	31104	0.00	18.34
31961	31961	0.00	16.94
31592	31592	0.00	19.93
32743	32743	0.00	20.92
30839	30839	0.00	21.54
31103	31103	0.00	20.70
31839	31839	0.00	17.64

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 2.3-2021-01

Validated substance/substance group	**Siam benzoin**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31490-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Siam benzoin

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Siam benzoin	3	2	0

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Siam benzoin*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Siam benzoin	3602151	31490	60	not required
Primavera	Siam benzoin	00051M23	31844	60	not required
Primavera	Siam benzoin	00074M26	34388	40	not required

Validation samples

A total of 53 906 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 *Siam benzoin*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Siam benzoin*.
- 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
Primavera	Siam benzoin	00218C24	32184	40
Primavera	Siam benzoin	00606B26	34171	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Siam benzoin*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Siam benzoin* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Siam benzoin* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	80	0	20 721
Type C	0	0	0	8600

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Siam benzoin* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cinnamon bark oil, Ceylon	103.67	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31844	31844	0.00	195.47
31490	31490	0.00	103.67
34388	34388	0.00	226.78

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 2.3-2021-01

Validated substance/substance group	**Solutio Cordes®**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30996-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Solutio Cordes®

Special notes

When selecting the *Solutio Cordes®* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Solutio Cordes®	2	3	16

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Solutio Cordes*®:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Ichthyol	Solutio Cordes®	12B006	30996	40	not required
Ichthyol	Solutio Cordes®	13B001	31076	40	not required

Validation samples

A total of 53 906 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 *Solutio Cordes*®. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Solutio Cordes*®.
- 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
Ichthyol	Solutio Cordes®	15B005	32065	60
Ichthyol	Solutio Cordes®	17B007	34361	40
Ichthyol	Solutio Cordes®	19B007	34845	40
Ichthyol	Solutio Cordes®	15B005	32483	40

- 20 621 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 66 spectra from 25 *Apo-Ident* customers from 20 batches from the substance/substance group *Solutio Cordes*®.

- 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
cordes hermann & co	Solutio Cordes®	16B010	2
Fiebig	Solutio Cordes®	22314	1
Gehe/Ichthyol	Solutio Cordes®	14b006	1
Ichthol/ Noweda 13.11.18	Solutio Cordes®	17b007	1
ichthyol	Solutio Cordes®	17B008	2
Ichthyol	Solutio Cordes®	12B005	1
Ichthyol / G	Solutio Cordes®	14B012	1
Ichthyol / G	Solutio Cordes®	16B005	3
Ichthyol / Gehe	Solutio Cordes®	14B006	1
Ichthyol / K	Solutio Cordes®	15B005	3
Ichthyol /Noweda	Solutio Cordes®	12B005	1
Ichthyol /Noweda	Solutio Cordes®	138002	1
Ichthyol Gesellschaft	Solutio Cordes®	14B006	1
Ichthyol Gesellschaft	Solutio Cordes®	14B012	1
Ichthyol- Gesellschaft ...	Solutio Cordes®	13B001	1
Ichthyol/AHCA	Solutio Cordes®	17B007	1
Ichthyol/Ph	Solutio Cordes®	17B007	1
Ichthyol/Phönix	Solutio Cordes®	12B0005	1
Ichthyol/Phönix	Solutio Cordes®	12B005	15
Ichthyol/Phönix	Solutio Cordes®	13B002	3
Ichthyol/Phönix	Solutio Cordes®	14B011	1
Ichthyol/Phönix	Solutio Cordes®	15B001	1
Ichthyol/Sanacorp	Solutio Cordes®	18B004	1
Ichthyol-Gesellschaft	Solutio Cordes®	15B005	1
Ichthyol-Gesellschaft	Solutio Cordes®	18B004	1
Ichthyol-Gesellschaft /...	Solutio Cordes®	18B004	1
Ichthyol-Gesellschaft /...	Solutio Cordes®	188004	1
Ichthyol-Gesellschaft C...	Solutio Cordes®	17B007	1
Ichthyol-Gesellschaft C...	Solutio Cordes®	18B004	1
Ichthyol-Gesellschaft/ ...	Solutio Cordes®	18B004	1
Ichthyol-Gesellschaft/ ...	Solutio Cordes®	18B004	1
Ichtyol	Solutio Cordes®	12B006	2
Ichtyol	Solutio Cordes®	13B002	1
Ichtyol-Gesellschaft	Solutio Cordes®	14B011	4
Ichtyol-Gesellschaft	Solutio Cordes®	15B001	2
ICHTYOL-GESELLSCHAFT	Solutio Cordes®	13B001	1
Phönix	Solutio Cordes®	13B002	1
Ichthyol	Solutio Cordes®	12B006	1
Ichthyol	Solutio Cordes®	13B001	1

- 8534 spectra from 735 *Apo-Ident* customers from a total of 3526 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Solutio Cordes*® can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Solutio Cordes*® and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	180	0	20 621
Type C	0	62	4	8534

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 96.6667 %)
Type C	100.0000 % (> 98.7858 %)	93.9394 % (> 89.3939 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

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

Substance	Distance in main model	Distance in second-stage model
Neuroderm® moisturising cream	71.23	–

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

Identity according to identity test using NIR spectroscopy

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

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30996	30996	0.00	77.28
31076	31076	0.00	78.25

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 2.3-2021-01

Validated substance/substance group	**Spearmint oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30453-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Spearmint oil; Oleum mentha spicata

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Spearmint oil	3	1	5

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Spearmint oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Spearmint oil	33894-111575BAG90451	31135	30	not required
Taoasis	Spearmint oil	946-120296	31685	60	not required
Taoasis	Spearmint oil	421012-129111	33481	40	not required

Validation samples

A total of 53 906 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 *Spearmint oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 375 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Spearmint oil*.
- 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
Taoasis	Spearmint oil	421012-126408	33200	40
Taoasis	Spearmint oil	421012-126408	33201	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 2 *Apo-Ident* customers from 5 batches from the substance/substance group *Spearmint oil*.
- 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
Taoasis	Spearmint oil	421012-123260	1
Taoasis	Spearmint oil	27537-96244	1
Taoasis	Spearmint oil	421012-125373	1
Taoasis	Spearmint oil	106555-973	1
Taoasis	Spearmint oil	106555-5139	1

- 8595 spectra from 736 *Apo-Ident* customers from a total of 3541 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Spearmint oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Spearmint oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 375
Type B	0	80	0	20 721
Type C	0	5	0	8595

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.3846 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7978 %)	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 *Spearmint oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Dwarf pine oil	48.51	–
Angelica root oil	55.62	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31135	31135	0.00	61.59
31685	31685	0.00	58.12
33481	33481	0.00	52.48

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 2.3-2021-01

Validated substance/substance group	**Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31032-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil; Frankincense oil; Oleum abies alba; Oleum boswellia serrata; Oleum pini sibiricum; Oleum pini silvestris; Pine silvestris oil; Silver fir oil; Spruce needle oil

Special notes

When selecting the *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Frankincense oil	4	4	2
Pine silvestris oil	2	3	2
Silver fir oil	4	1	2
Spruce needle oil	3	4	17

Second-stage model

For differentiation of the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Frankincense oil	15181-119714	31633	60	not required
Taoasis	Frankincense oil	1509-125625	33052	40	not required
Taoasis	Frankincense oil	4314-129238	33646	40	not required
Taoasis	Frankincense oil	1500910-128786	33650	40	not required
Taoasis	Frankincense oil	1500910-128786	33652	40	not required
Primavera	Pine silvestris …	00664E26	34177	40	not required
Taoasis	Pine silvestris …	1790-129074	33815	30	not required
Primavera	Silver fir oil	00287M26	34391	40	not required
Taoasis	Silver fir oil	120830-111781	31032	40	not required
Taoasis	Silver fir oil	211-114751	31255	40	not required
Taoasis	Silver fir oil	01A0B15-121623	31754	60	not required
Taoasis	Spruce needle oil	1507-122520	31819	60	not required
Taoasis	Spruce needle oil	1719-124011	32066	60	not required
Taoasis	Spruce needle oil	10213-149	33726	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 630 spectra of 14 reference samples from the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 13 different batches.

- 23 875 spectra from a total of 491 batches from further 157 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples:

In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 550 spectra of 14 reference samples from the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil*.

- 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
Primavera	Frankincense oil	00446M26	34400	40
Taoasis	Frankincense oil	3.26550	30843	40
Taoasis	Frankincense oil	1509-122197	31820	60
Taoasis	Frankincense oil	2124-2905	34277	40
Primavera	Pine silvestris oil	00398J26	34292	40
Primavera	Pine silvestris oil	00028A27	34378	40
Taoasis	Pine silvestris oil	1790-125357BAG90451	33829	40
Taoasis	Silver fir oil	01A0B16-125623	33026	40
Caelo	Spruce needle oil	11220801	30613	40
Taoasis	Spruce needle oil	29828-103169BAG90451	30672	40
Taoasis	Spruce needle oil	1769-124969	32479	40
Taoasis	Spruce needle oil	11647-2942	34112	40
Taoasis	Pine silvestris oil	1790-129074	33815†	10
Taoasis	Silver fir oil	01A0B16-125623	33027	40

- 20 251 spectra from a total of 434 batches from further 200 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 13 *Apo-Ident* customers from 24 batches from the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil*.

- 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
Apoth.Bauer&Co/Noweda	Frankincense oil	3175391505	1
Taoasis	Frankincense oil	549702-112299	1
Taoasis	Pine silvestris oil	1940-5617	1
Taoasis	Pine silvestris oil	1940-6527	1
Taoasis	Silver fir oil	212-120342	1
Taoasis	Silver fir oil	30447-125444	1
Caelo	Spruce needle oil	11324401	4
Caelo	Spruce needle oil	10185604	1
Caelo	Spruce needle oil	13152001	2
Primavera	Spruce needle oil	1670814	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
Taoasis	Spruce needle oil	29828-107964	1
Taoasis	Spruce needle oil	534474-111585	1
Taoasis	Spruce needle oil	531766-109893	1
Taoasis	Spruce needle oil	534374-22869	1
Taoasis	Spruce needle oil	442-113922	1
Taoasis	Spruce needle oil	1769-124949	1
Taoasis	Spruce needle oil	1769-124969	2
Taoasis	Spruce needle oil	1769-127000	2
Taoasis	Spruce needle oil	11647-1921	3
Taoasis	Spruce needle oil	114780-6023	1
Taoasis/Sanacorp	Spruce needle oil	534474-111869	1
Taoasis/Sanacorp	Spruce needle oil	534474-113171	1
Taoasis/Sanacorp	Spruce needle oil	11647-2942	1
Apoth.Bauer&Co/Noweda	Frankincense oil		1

- 8568 spectra from 736 *Apo-Ident* customers from a total of 3522 batches from a further 146 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

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

	False positive	True positive	False negative	True negative
Type A	0	630	0	23 875
Type B	0	403	147	20 251
Type C	0	17	15	8568

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9600 %)	100.0000 % (> 99.0476 %)
Type B	100.0000 % (> 99.9453 %)	73.2727 % (> 72.7273 %)
Type C	100.0000 % (> 98.7868 %)	53.1250 % (> 43.7500 %)

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Swiss pine oil	12.39	–
Spearmint oil	20.79	–
Dwarf pine oil	26.76	–
Angelica root oil	26.96	–
Ginger oil	29.41	–
Citus oil	29.54	–
Hyssop oil	32.48	–
Citric oil	33.78	–
Marjoram oil	34.60	–
Juniper oil	38.47	–
Cypress oil	40.46	–
Myrtle oil	40.74	–
Lime oil	41.68	–
Cumin oil	49.11	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
34177	34177	0.00	19.59
32066	32066	0.00	19.55
33052	33052	0.00	33.75
31633	31633	0.00	74.79
31754	31754	0.00	21.95
33650	33650	0.00	86.74
33652	33652	0.00	84.73
33815	33815	0.00	15.80
33646	33646	0.00	13.67
31819	31819	0.00	16.94
34391	34391	0.00	41.68
31032	31032	0.00	32.48
31255	31255	0.00	35.31
33726	33726	0.00	12.39

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 2.3-2021-01

Validated substance/substance group	**Stomahesive® adhesive paste**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30974-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Stomahesive® adhesive paste

Special notes

When selecting the *Stomahesive® adhesive paste* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

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

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Stomahesive® adhesive paste	3	2	5

Second-stage model

For differentiation of the substance/substance group *Stomahesive®* *adhesive paste* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Stomahesive®* *adhesive paste*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
ConvaTec Inc.	Stomahesive® adh…	2D117	30974	80	not required
ConvaTec Inc.	Stomahesive® adh…	2M084	31087	40	not required
ConvaTec Inc.	Stomahesive® adh…	6L039	33474	40	not required

Validation samples

A total of 53 906 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 *Stomahesive®* *adhesive paste*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Stomahesive®* *adhesive paste*.
- 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
ConvaTec Inc.	Stomahesive® adhesive paste	6D079	32761	40
ConvaTec Inc.	Stomahesive® adhesive paste	5G062	32954	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 7 *Apo-Ident* customers from 5 batches from the substance/substance group *Stomahesive® adhesive paste*.
- 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
Apomix/Gehe	Stomahesive® adhesive paste	9B033	2
Convatec	Stomahesive® adhesive paste	5G062	24
ConvaTec/ Alliance	Stomahesive® adhesive paste	9K007	2
Convatec/Gehe	Stomahesive® adhesive paste	9D046	1
Convatec/Phönix	Stomahesive® adhesive paste	6D079	1

- 8570 spectra from 736 *Apo-Ident* customers from a total of 3541 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Stomahesive® adhesive paste* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Stomahesive® adhesive paste* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	80	0	20 721
Type C	0	30	0	8570

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7869 %)	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 *Stomahesive®* *adhesive paste* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Lygal® head ointment N 3%	40.76	–
Lygal® ointment base	61.86	–

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

Identity according to identity test using NIR spectroscopy

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

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30974	30974	0.00	52.31
31087	31087	0.00	55.77
33474	33474	0.00	56.05

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 2.3-2021-01

Validated substance/substance group	**Strawberry aroma**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30643-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Strawberry aroma; Strawberry flavour

Special notes

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

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

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

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

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

Number of independent samples (batches) in calibration and validation

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

Substance	Type A	Type B	Type C
Strawberry aroma	3	4	25

Second-stage model

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

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Strawberry aroma*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Strawberry aroma	11178804	30643	40	1402439
Caelo	Strawberry aroma	13252407	31395	40	not required
Caelo	Strawberry aroma	15411807	32814	40	not required
Caelo	Strawberry aroma	15411807	32838	40	1704074

Validation samples

A total of 53 906 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 *Strawberry aroma*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 345 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Strawberry aroma*.
- 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	Strawberry aroma	14311215	32567	40

continued on the next page

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Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Strawberry aroma	170246	33056	40
Caelo	Strawberry aroma	180832	34077	40
Caelo	Strawberry aroma	192763004	35142	40
Caelo	Strawberry aroma	14311215	32837	40

- 20 601 spectra from a total of 443 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

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

- 81 spectra from 54 *Apo-Ident* customers from 27 batches from the substance/substance group *Strawberry aroma*.

- 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	Strawberry aroma	12183504	2
Caelo	Strawberry aroma	13252405	1
Caelo	Strawberry aroma	12183511	1
Caelo	Strawberry aroma	9101405	1
Caelo	Strawberry aroma	13252417	1
Caelo	Strawberry aroma	15411813	4
Caelo	Strawberry aroma	17024604	5
Caelo	Strawberry aroma	10803202	1
Caelo	Strawberry aroma	17024607	1
Caelo	Strawberry aroma	10184917	1
Caelo	Strawberry aroma	18083206	4
Caelo	Strawberry aroma	15411805	7
Caelo	Strawberry aroma	18083215	2
Caelo	Strawberry aroma	14311209	5
Caelo	Strawberry aroma	14311204	1
Caelo	Strawberry aroma	18083202	7
Caelo	Strawberry aroma	17024606	7
Caelo	Strawberry aroma	11178813	1
Caelo	Strawberry aroma	13252409	2
Caelo	Strawberry aroma	12183513	4
Caelo	Strawberry aroma	17024608	6
Caelo	Strawberry aroma	14311215	2
Caesar & Loretz GmbH	Strawberry aroma	18083211	2
Caesar & Loretz GmbH	Strawberry aroma	18083215	1
Caesar & Loretz GmbH	Strawberry aroma	18083208	1
Caesar & Loretz GmbH / ...	Strawberry aroma	18083206	1
Caesar & Loretz GmbH/Je...	Strawberry aroma	18083211	1
Gehe	Strawberry aroma	17024606	1
Hedinger	Strawberry aroma	14311215	1
noweda	Strawberry aroma	192763002	1
Caelo	Strawberry aroma	13252407	2
Caelo	Strawberry aroma	15411807	4

- 8519 spectra from 734 *Apo-Ident* customers from a total of 3519 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Strawberry aroma* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Strawberry aroma* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 345
Type B	0	200	0	20 601
Type C	0	81	0	8519

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

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 96.2500 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.7856 %)	100.0000 % (> 92.5926 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Strawberry aroma* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Raspberry aroma	59.87	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Strawberry aroma* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31395	31395	0.00	79.69
30643	30643	0.00	98.19
32814	32814	0.00	91.58
32838	32838	0.00	65.64

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 2.3-2021-01

Validated substance/substance group	**Swiss pine oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31553-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Swiss pine oil; Oleum pinus cembra

Special notes

When selecting the *Swiss pine oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Swiss pine oil	4	2	2

Second-stage model

For differentiation of the substance/substance group *Swiss pine oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Swiss pine oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Swiss pine oil	4892-117271	31553	60	not required
Taoasis	Swiss pine oil	3023-120087	31680	60	not required
Taoasis	Swiss pine oil	12069-127103	32934	40	not required
Taoasis	Swiss pine oil	10304-128929	33645	40	not required

Validation samples

A total of 53 906 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 *Swiss pine oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Swiss pine oil*.
- 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
Primavera	Swiss pine oil	00661A27	34386	40
Taoasis	Swiss pine oil	201610159-126370	32793	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Swiss pine oil*.

- 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	Swiss pine oil	6158653	1
Oswald	Swiss pine oil	9971217	1

- 8598 spectra from 736 *Apo-Ident* customers from a total of 3544 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Swiss pine oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Swiss pine oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	40	40	20 721
Type C	0	2	0	8598

The substance/substance group *Swiss pine oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	50.0000 % (> 46.2500 %)
Type C	100.0000 % (> 98.8173 %)	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 *Swiss pine oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Frankincense oil	14.37	–
Pine silvestris oil	19.21	–
Spruce needle oil	20.64	–
Angelica root oil	22.16	–
Silver fir oil	23.42	–
Dwarf pine oil	25.38	–
Spearmint oil	26.37	–
Ginger oil	31.67	–
Citus oil	34.12	–
Cypress oil	38.10	–
Marjoram oil	39.94	–
Juniper oil	55.80	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Swiss pine oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31553	31553	0.00	20.72
32934	32934	0.00	28.99
31680	31680	0.00	14.37
33645	33645	0.00	17.44

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 2.3-2021-01

Validated substance/substance group	**Tea tree oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30959-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Tea tree oil; Oleum melaleuca alternifolia

Special notes

When selecting the *Tea tree oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Tea tree oil	3	3	23

Second-stage model

For differentiation of the substance/substance group *Tea tree oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Tea tree oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Tea tree oil	533902-109942BAG91303	30959	40	not required
Taoasis	Tea tree oil	34828-113642BAG91303	31134	40	not required
Taoasis	Tea tree oil	44737-121997	31762	60	not required

Validation samples

A total of 53 906 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 *Tea tree oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 3 different batches.
- 24 365 spectra from a total of 501 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Tea tree oil*.
- 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
Primavera	Tea tree oil	00667A27	34396	40
Taoasis	Tea tree oil	52642-125539	33017	40
Taoasis	Tea tree oil	52642-124527	33018	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 *Apo-Ident* customers from 23 batches from the substance/substance group *Tea tree oil*.

- 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	Tea tree oil	15337112	1
Caelo	Tea tree oil	15337105	1
Caelo	Tea tree oil	15051806	2
Caelo	Tea tree oil	15051807	1
Caelo	Tea tree oil	15337106	1
Taoasis	Tea tree oil	20269-116833	2
Taoasis	Tea tree oil	1469-117418	2
Taoasis	Tea tree oil	20269-117745G09	1
Taoasis	Tea tree oil	28348-121597	2
Taoasis	Tea tree oil	28348-121515	1
Taoasis	Tea tree oil	28348-119841	1
Taoasis	Tea tree oil	52642-124559	1
Taoasis	Tea tree oil	52642-124919	1
Taoasis	Tea tree oil	52642-12078	1
Taoasis	Tea tree oil	52642-125539BAG91303	12
Taoasis	Tea tree oil	76283-778	1
Taoasis	Tea tree oil	76283-129307	2
Taoasis	Tea tree oil	128919-AUJ07	1
Taoasis	Tea tree oil	90725-2423	1
Taoasis	Tea tree oil	92962-3613	1
Taoasis	Tea tree oil	92962-3626	2
Taoasis	Tea tree oil	92962-5142	3
Taoasis/Taoasis	Tea tree oil	JF20461-1972	1

- 8558 spectra from 736 *Apo-Ident* customers from a total of 3523 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Tea tree oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Tea tree oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 365
Type B	0	120	0	20 681
Type C	0	42	0	8558

The substance/substance group *Tea tree oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9603 %)	100.0000 % (> 95.7143 %)
Type B	100.0000 % (> 99.9455 %)	100.0000 % (> 95.0000 %)
Type C	100.0000 % (> 98.7863 %)	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 *Tea tree oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Marjoram oil	19.85	–
Carrot seed oil	44.55	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Tea tree oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30959	30959	0.00	51.68
31134	31134	0.00	53.94
31762	31762	0.00	59.09

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 2.3-2021-01

Validated substance/substance group	**Thuja oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33828-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Thuja oil; Thuja (essential oil)

Special notes

When selecting the *Thuja oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Thuja oil	2	1	0

Second-stage model

For differentiation of the substance/substance group *Thuja oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Thuja oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Thuja oil	66255-969	33828	40	not required
Taoasis	Thuja oil	66255-2932	34287	40	not required

Validation samples

A total of 53 906 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 *Thuja oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Thuja oil*.
- 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
Taoasis	Thuja oil	28508-121881	34038	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Thuja oil*.
- 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.
- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Thuja oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thuja oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	40	0	20 761
Type C	0	0	0	8600

The substance/substance group *Thuja oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.8097 %)	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 *Thuja oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cumin oil	45.87	–
Common wormwood oil	63.86	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thuja oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33828	33828	0.00	44.51
34287	34287	0.00	47.66

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 2.3-2021-01

Validated substance/substance group	**Thyme oil, red**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30929-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Thyme oil, red; Oleum thymus vulgaris

Special notes

When selecting the *Thyme oil, red* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Thyme oil, red	5	1	19

Second-stage model

For differentiation of the substance/substance group *Thyme oil, red* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Thyme oil, red*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Thyme oil, red	31911-109378	30929	40	not required
Taoasis	Thyme oil, red	9434-115427	31259	40	not required
Taoasis	Thyme oil, red	56081-124964	32482	40	not required
Taoasis	Thyme oil, red	1829-125364	32981	40	not required
Taoasis	Thyme oil, red	1976-2943	34103	40	not required

Validation samples

A total of 53 906 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 *Thyme oil, red*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.
- 24 305 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Thyme oil, red*.
- 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
Taoasis	Thyme oil, red	40517-121881	32472	40

- 20 761 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 4 *Apo-Ident* customers from 19 batches from the substance/substance group *Thyme oil, red*.

- 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
Caesar & Loretz GmbH	Thyme oil, red	5841	1
Taoasis	Thyme oil, red	33092-111620	1
Taoasis	Thyme oil, red	14381-117385	1
Taoasis	Thyme oil, red	25394-118296	1
Taoasis	Thyme oil, red	9434-115525	1
Taoasis	Thyme oil, red	32444-118785	4
Taoasis	Thyme oil, red	40517-121881	2
Taoasis	Thyme oil, red	33635-120088	1
Taoasis	Thyme oil, red	43637-122713	1
Taoasis	Thyme oil, red	43637-122852	1
Taoasis	Thyme oil, red	43637-123574	1
Taoasis	Thyme oil, red	43637-124964	1
Taoasis	Thyme oil, red	56081-126921	1
Taoasis	Thyme oil, red	56081-127214	1
Taoasis	Thyme oil, red	1976-3100	2
Taoasis	Thyme oil, red	1976-3455	1
Taoasis	Thyme oil, red	1976-5867	2
Taoasis	Thyme oil, red	1976-5865	1
Taoasis	Thyme oil, red	1976-6717	1
Taoasis/Sanacorp	Thyme oil, red	1976-3455	1

- 8574 spectra from 736 *Apo-Ident* customers from a total of 3527 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Thyme oil, red* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thyme oil, red* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	40	0	20 761
Type C	0	22	4	8574

The substance/substance group *Thyme oil, red* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9460 %)	100.0000 % (> 85.0000 %)
Type C	100.0000 % (> 98.7873 %)	84.6154 % (> 73.0769 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Thyme oil, red* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Savory herb	19.59	–
Oregano oil	22.08	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thyme oil, red* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30929	30929	0.00	26.43
34103	34103	0.00	28.04
31259	31259	0.00	21.62
32482	32482	0.00	33.45
32981	32981	0.00	24.84

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 2.3-2021-01

Validated substance/substance group	**Thyme oil, white / Coriander oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31552-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Thyme oil, white / Coriander oil; Coriander oil; Oleum coriandri; Thyme oil, white

Special notes

When selecting the *Thyme oil, white / Coriander oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Coriander oil	4	2	9
Thyme oil, white	3	3	0

Second-stage model

For differentiation of the substance/substance group *Thyme oil, white / Coriander oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Thyme oil, white / Coriander oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Coriander oil	9324-114961	31552	60	not required
Taoasis	Coriander oil	25134-117444	31690	60	not required
Taoasis	Coriander oil	104709-126301	32792	40	not required
Taoasis	Coriander oil	109291-2941	34286	40	not required
Primavera	Thyme oil, white	01067J25	33796	40	not required
Primavera	Thyme oil, white	00593E26	34176	40	not required
Taoasis	Thyme oil, white	111400-970	33818	40	not required

Validation samples

A total of 53 906 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 *Thyme oil, white / Coriander oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 7 different batches.

- 24 185 spectra from a total of 497 batches from further 159 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Thyme oil, white / Coriander oil*.

- 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
Taoasis	Coriander oil	104709-127188	33053	40
Taoasis	Coriander oil	9291-1307	33990	40
Primavera	Thyme oil, white	00146J26	34293	40
Primavera	Thyme oil, white	00535M26	34369	40
Taoasis	Thyme oil, white	925	33819	40

- 20 601 spectra from a total of 442 batches from further 202 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 9 *Apo-Ident* customers from 9 batches from the substance/substance group *Thyme oil, white / Coriander oil*.

- 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
Apotheker Bauer & Cie. ...	Coriander oil	8008-52-4	1
Caelo	Coriander oil	15229607	1
Caelo	Coriander oil	17050408	1
Caelo	Coriander oil	16140401	1
Caesar & Loretz GmbH	Coriander oil	19081003	1
GEHE	Coriander oil	17050403	1
Sanacorp	Coriander oil	18125703	1
taoasis	Coriander oil	104709127	1
Taoasis	Coriander oil	9291-1307	1

- 8591 spectra from 735 *Apo-Ident* customers from a total of 3537 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Thyme oil, white / Coriander oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Thyme oil, white / Coriander oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 185
Type B	0	200	0	20 601
Type C	0	9	0	8591

The substance/substance group *Thyme oil, white / Coriander oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 98.1250 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 97.0000 %)
Type C	100.0000 % (> 98.7920 %)	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 *Thyme oil, white / Coriander oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Matricaria oil, morrocan	20.15	–
Rosewood oil	46.63	–
Carrot seed oil	52.81	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Thyme oil, white / Coriander oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31690	31690	0.00	69.07
34286	34286	0.00	55.53
33796	33796	0.00	37.32
34176	34176	0.00	40.09
31552	31552	0.00	57.64
33818	33818	0.00	60.99
32792	32792	0.00	59.95

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 2.3-2021-01

Validated substance/substance group	**Vetiver bourbon oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	`31546-2021-03-22`
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Vetiver bourbon oil; Oleum vetiveria zizanoides

Special notes

When selecting the *Vetiver bourbon oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Vetiver bourbon oil	4	1	9

Second-stage model

For differentiation of the substance/substance group *Vetiver bourbon oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Vetiver bourbon oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Vetiver bourbon …	7141-116418	31546	60	not required
Taoasis	Vetiver bourbon …	7141-119962	31684	60	not required
Taoasis	Vetiver bourbon …	7141-128198	33647	40	not required
Taoasis	Vetiver bourbon …	1710-48621A-11231	35143	40	not required

Validation samples

A total of 53 906 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 *Vetiver bourbon oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Vetiver bourbon oil*.
- 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
Taoasis	Vetiver bourbon oil	7141-124922	32810	40
Taoasis	Vetiver bourbon oil	7141-124922	33046	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 1 *Apo-Ident* customers from 9 batches from the substance/substance group *Vetiver bourbon oil*.

- 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
Taoasis	Vetiver bourbon oil	7141-124600	2
Taoasis	Vetiver bourbon oil	7141-119174	1
Taoasis	Vetiver bourbon oil	7141-122195	2
Taoasis	Vetiver bourbon oil	7141-123924	1
Taoasis	Vetiver bourbon oil	7141-137885	1
Taoasis	Vetiver bourbon oil	108-232	1
Taoasis	Vetiver bourbon oil	2060-1665	2
Taoasis	Vetiver bourbon oil	2060-5667	4
Taoasis	Vetiver bourbon oil	2060-3449	1

- 8585 spectra from 736 *Apo-Ident* customers from a total of 3537 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Vetiver bourbon oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Vetiver bourbon oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	80	0	20 721
Type C	0	15	0	8585

The substance/substance group *Vetiver bourbon oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7891 %)	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 *Vetiver bourbon oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citus oil	28.35	–
Myrtle oil	29.47	–
Immortelle oil	30.41	–
Manuka oil	33.39	–
Patchouli oil	35.09	–
Rose-geranium oil, organic	35.40	–
Carrot seed oil	38.31	–
Lemon grass oil	38.92	–
Ginger oil	39.48	–
Hyssop oil	42.68	–
Marjoram oil	44.90	–
Tea tree oil	47.87	–
Cypress oil	52.78	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Vetiver bourbon oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31684	31684	0.00	31.44
33647	33647	0.00	31.82
35143	35143	0.00	35.09
31546	31546	0.00	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 2.3-2021-01

Validated substance/substance group	**Wart ointment InfectoPharm® (NRF 11.31)**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30730-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Wart ointment InfectoPharm® (NRF 11.31)

Special notes

When selecting the *Wart ointment InfectoPharm® (NRF 11.31)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wart ointment InfectoPharm® (NRF 11.31)	2	3	42

Second-stage model

For differentiation of the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Infectopharm	Wart ointment In…	S031201.1	30730	40	not required
Infectopharm	Wart ointment In…	S031201.1	30905	40	not required
Infectopharm	Wart ointment In…	S121103.1	30906	40	not required

Validation samples

A total of 53 906 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 *Wart ointment InfectoPharm® (NRF 11.31)*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 385 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Wart ointment InfectoPharm® (NRF 11.31)*.
- 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
Infectopharm	Wart ointment InfectoPharm® …	S021601.1	32593	40
Infectopharm	Wart ointment InfectoPharm® …	S071602.1	32953	40
Infectopharm	Wart ointment InfectoPharm® …	S061801.1	34517	40

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Supplier	Substance	Batch	Sample ID	Spectra
Infectopharm	Wart ointment InfectoPharm® ...	S071602.1	33515	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 220 spectra from 95 *Apo-Ident* customers from 52 batches from the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)*.

- 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	Wart ointment InfectoPharm® ...	S111202	1
Caelo	Wart ointment InfectoPharm® ...	s0617012	1
Caelo	Wart ointment InfectoPharm® ...	S0215011	3
infectopharm	Wart ointment InfectoPharm® ...	S0211604	1
Infectopharm	Wart ointment InfectoPharm® ...	3013I-07003	1
Infectopharm	Wart ointment InfectoPharm® ...	S041301	1
Infectopharm	Wart ointment InfectoPharm® ...	S111202	1
InfectoPharm	Wart ointment InfectoPharm® ...	S0215011	1
InfectoPharm	Wart ointment InfectoPharm® ...	s061801	1
Infectopharm / Phönix	Wart ointment InfectoPharm® ...	4117A-03898	1
Infectopharm / Phönix	Wart ointment InfectoPharm® ...	3718A-03898	1
Infectopharm GmbH	Wart ointment InfectoPharm® ...	s061801-1	1
Infectopharm/AHD	Wart ointment InfectoPharm® ...	S1219021	1
InfectoPharm/Anzag	Wart ointment InfectoPharm® ...	716A-03898	1
Infectopharm/Noweda	Wart ointment InfectoPharm® ...	S0716021	1
Infectopharm/Römer/Noweda	Wart ointment InfectoPharm® ...	S0215011	2
Infectopharm/Spangro	Wart ointment InfectoPharm® ...	S061801-1	1
Löwen City-Apotheke Bar...	Wart ointment InfectoPharm® ...	8032013	1
AHD	Wart ointment InfectoPharm® ...		1
Caelo	Wart ointment InfectoPharm® ...		3
Eigenherstellung	Wart ointment InfectoPharm® ...		1
Euro OTC	Wart ointment InfectoPharm® ...		1
Fagron	Wart ointment InfectoPharm® ...		4
Gehe	Wart ointment InfectoPharm® ...		1
GEHE	Wart ointment InfectoPharm® ...		3
gehe/infecto	Wart ointment InfectoPharm® ...		1
Ichthyol-Gesellschaft C...	Wart ointment InfectoPharm® ...		1
Infec/ Phönix	Wart ointment InfectoPharm® ...		1
Infect/PX	Wart ointment InfectoPharm® ...		2
infectipharm/Phönix	Wart ointment InfectoPharm® ...		1
Infecto Pharm / Noweda	Wart ointment InfectoPharm® ...		4
Infecto/Gehe	Wart ointment InfectoPharm® ...		1
Infecto/Spangro	Wart ointment InfectoPharm® ...		1
Infectoph./Gehe	Wart ointment InfectoPharm® ...		1
Infectoph./Kehr	Wart ointment InfectoPharm® ...		1
infectopharm	Wart ointment InfectoPharm® ...		3
Infectopharm	Wart ointment InfectoPharm® ...		52

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Supplier	Substance	Batch	Spectra
InfectoPharm	Wart ointment InfectoPharm® ...		14
Infectopharm (Phoenix)	Wart ointment InfectoPharm® ...		1
Infectopharm / Alliance	Wart ointment InfectoPharm® ...		1
Infectopharm / Alliance...	Wart ointment InfectoPharm® ...		1
InfectoPharm / Alliance...	Wart ointment InfectoPharm® ...		2
Infectopharm / Gehe	Wart ointment InfectoPharm® ...		1
InfectoPharm / Gehe	Wart ointment InfectoPharm® ...		1
Infectopharm / Phoenix	Wart ointment InfectoPharm® ...		1
Infectopharm / Phönix	Wart ointment InfectoPharm® ...		1
Infectopharm / Sanacorp	Wart ointment InfectoPharm® ...		1
Infectopharm Arzneimittel	Wart ointment InfectoPharm® ...		10
Infectopharm Arzneimitt...	Wart ointment InfectoPharm® ...		1
INFECTOPHARM -Noweda	Wart ointment InfectoPharm® ...		1
Infectopharm/	Wart ointment InfectoPharm® ...		1
Infectopharm/ Alliance	Wart ointment InfectoPharm® ...		1
InfectoPharm/ E	Wart ointment InfectoPharm® ...		1
Infectopharm/ Noweda	Wart ointment InfectoPharm® ...		3
Infectopharm/ Sanacorp	Wart ointment InfectoPharm® ...		1
InfectoPharm/AHD	Wart ointment InfectoPharm® ...		1
Infectopharm/Alliance H...	Wart ointment InfectoPharm® ...		1
Infectopharm/AllianceHe...	Wart ointment InfectoPharm® ...		1
Infectopharm/Allianz	Wart ointment InfectoPharm® ...		4
Infectopharm/Anzag	Wart ointment InfectoPharm® ...		1
InfectoPharm/Anzag	Wart ointment InfectoPharm® ...		2
Infectopharm/Ebert	Wart ointment InfectoPharm® ...		1
InfectoPharm/Fiebig	Wart ointment InfectoPharm® ...		1
Infectopharm/G	Wart ointment InfectoPharm® ...		1
Infectopharm/Gehe	Wart ointment InfectoPharm® ...		10
Infectopharm/GEHE	Wart ointment InfectoPharm® ...		1
InfectoPharm/Gehe	Wart ointment InfectoPharm® ...		1
InfectoPharm/GEHE	Wart ointment InfectoPharm® ...		1
INFECTOPHARM/GEHE 02.05...	Wart ointment InfectoPharm® ...		1
INFECTOPHARM/GEHE 07.07...	Wart ointment InfectoPharm® ...		1
INFECTOPHARM/GEHE 28.09...	Wart ointment InfectoPharm® ...		1
Infectopharm/K	Wart ointment InfectoPharm® ...		1
Infectopharm/Kehr	Wart ointment InfectoPharm® ...		1
Infectopharm/Noweda	Wart ointment InfectoPharm® ...		10
InfectoPharm/Noweda	Wart ointment InfectoPharm® ...		3
Infectopharm/Phoenix	Wart ointment InfectoPharm® ...		2
InfectoPharm/Phoenix	Wart ointment InfectoPharm® ...		6
Infectopharm/Phoenix Le...	Wart ointment InfectoPharm® ...		1
Infectopharm/Phönix	Wart ointment InfectoPharm® ...		7
InfectoPharm/Phönix	Wart ointment InfectoPharm® ...		1
InfectoPharma	Wart ointment InfectoPharm® ...		1
InfectopharmNoweda	Wart ointment InfectoPharm® ...		1
Infectophsrm	Wart ointment InfectoPharm® ...		1
nfectoPharm	Wart ointment InfectoPharm® ...		1
Noweda	Wart ointment InfectoPharm® ...		1
Noweda/infectopharm	Wart ointment InfectoPharm® ...		1
Noweda/Infectopharm	Wart ointment InfectoPharm® ...		1
Phönix Gotha	Wart ointment InfectoPharm® ...		1
Phönix/ Infectopharm	Wart ointment InfectoPharm® ...		1
Sanacorp	Wart ointment InfectoPharm® ...		2
Sanacorp/Infectopharm	Wart ointment InfectoPharm® ...		1

- 8380 spectra from 726 *Apo-Ident* customers from a total of 3495 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the

samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wart ointment InfectoPharm® (NRF 11.31)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 385
Type B	0	160	0	20 641
Type C	0	213	7	8380

The substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9604 %)	100.0000 % (> 95.0000 %)
Type B	100.0000 % (> 99.9454 %)	100.0000 % (> 96.2500 %)
Type C	100.0000 % (> 98.7851 %)	96.8182 % (> 95.4545 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Salicylic white paraffin 10%	137.23	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wart ointment InfectoPharm® (NRF 11.31)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
30906	30906	0.00	218.97
30730	30730	0.00	222.07
30905	30905	0.00	220.89

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 2.3-2021-01

Validated substance/substance group	**Water and aqueous solutions**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31047-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Water and aqueous solutions; Aloe Vera gel, 1:1; Aloe vera gel, 10x concentrated; Aqua; Bepanthen® solution; Retterspitz external; SyrSpend® SF pH4 cherry aroma; SyrSpend® SF pH4 aroma free; Water

Special notes

When selecting the *Water and aqueous solutions* substance/substance group, the following information is displayed to the user:

- Advice for the identification of water: Preserved, purified and distilled water can not be conclusively distinguished by spectral analysis. An additional analysis of identity may be required.

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Aloe Vera gel, 1:1	3	7	8
Aloe vera gel, 10x concentrated	4	3	2
Bepanthen® solution	3	2	2

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Substance	Type A	Type B	Type C
Retterspitz external	3	2	2
SyrSpend® SF pH4 cherry aroma	2	2	47
SyrSpend® SF pH4 aroma free	3	1	38
Water	4	23	138

Second-stage model

For differentiation of the substance/substance group *Water and aqueous solutions* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Water and aqueous solutions*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Aloe Vera gel, 1:1	13025802	31145	40	not required
Caelo	Aloe Vera gel, 1:1	15329203	31866	60	not required
Caelo	Aloe Vera gel, 1:1	153292	31880	60	20151111*
Caelo	Aloe Vera gel, 1:1	153292	31881	60	20151111*
Caelo	Aloe vera gel, 1...	13045901	31146	40	not required
Caelo	Aloe vera gel, 1...	15185503	31862	60	not required
Caelo	Aloe vera gel, 1...	161922	32313	40	20160707*
Caelo	Aloe vera gel, 1...	20001962	35049	40	20200702*
Bayer	Bepanthen® solut...	KP08DR1	31047	40	not required
Bayer	Bepanthen® solut...	KP0ASHC	31857	60	not required
Bayer	Bepanthen® solut...	KP0C3FU	33612	40	not required
Retterspitz G...	Retterspitz exte...	016100	32785	40	not required
Retterspitz G...	Retterspitz exte...	017058	33430	40	not required
Retterspitz G...	Retterspitz exte...	016240	33431	40	not required
Fagron	SyrSpend® SF pH4...	1503D017	31671	60	not required
Fagron	SyrSpend® SF pH4...	1503D017	31723	60	not required
Fagron	SyrSpend® SF pH4...	1704492/1	33787	40	not required
Fagron	SyrSpend® SF pH4...	1503D009	31670	60	not required
Fagron	SyrSpend® SF pH4...	1412D002	31722	60	not required
Fagron	SyrSpend® SF pH4...	19011410	35077	40	not required
Caelo	Water	15068701	31675	45	not required
Caelo	Water	153943	32079	40	20151215*
Caelo	Water	191968	34767	40	20190815*
Hedinger	Water	219066	31623	60	not required

Validation samples

A total of 53 906 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.

- 1165 spectra of 24 reference samples from the substance/substance group *Water and aqueous solutions*. These samples are listed above in the *calibration samples* section. The reference samples come from 22 different batches.

- 23 340 spectra from a total of 482 batches from further 154 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there was at least one additional sample (other sales container, other sample ID) from which reference spectra (*Type A*) were included in the database structure.

- 1645 spectra of 42 reference samples from the substance/substance group *Water and aqueous solutions*.

- Among them are spectra of independent samples from 40 batches from which no spectra 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	Aloe Vera gel, 1:1	162489	32580	40
Caelo	Aloe Vera gel, 1:1	162912	32899	40
Caelo	Aloe Vera gel, 1:1	171341	33411	40
Caelo	Aloe Vera gel, 1:1	172891	33736	40
Caelo	Aloe Vera gel, 1:1	172890	33970	40
Caelo	Aloe Vera gel, 1:1	181943	34251	40
Caelo	Aloe Vera gel, 1:1	191914	34764	40
Caelo	Aloe vera gel, 10x concentra…	17082002	33511	40
Caelo	Aloe vera gel, 10x concentra…	181255	34342	40
Caelo	Aloe vera gel, 10x concentra…	192411	34714	40
Bayer	Bepanthen® solution	KP0B60L	32719	40
Bayer	Bepanthen® solution	KP0BJ61	32949	40
Retterspitz GmbH	Retterspitz external	016179	32784	30
Retterspitz GmbH	Retterspitz external	017192	34049	40
Fagron	SyrSpend® SF pH4 cherry aroma	1503255	32738	40
Fagron	SyrSpend® SF pH4 cherry aroma	1603252/2	32842	40
Fagron	SyrSpend® SF pH4 aroma free	1704493	33501	40
Caelo	Water	153944	32081	40
Caelo	Water	153712	32083	40
Caelo	Water	162553	32895	40
Caelo	Water	162867	32896	40
Caelo	Water	163533	33176	40
Caelo	Water	170018	33177	40
Caelo	Water	172191	33578	40
Caelo	Water	172192	33579	40
Caelo	Water	172220	33580	40
Caelo	Water	172533	33741	40
Caelo	Water	172827	33742	40
Caelo	Water	172861	33743	40
Caelo	Water	172862	33744	40

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Supplier	Substance	Batch	Sample ID	Spectra
Caelo	Water	172771	33745	40
Caelo	Water	171147	33977	40
Caelo	Water	172957	33978	40
Caelo	Water	180045	34136	40
Caelo	Water	181105	34137	40
Caelo	Water	181354	34139	40
Caelo	Water	182286	34243	40
Caelo	Water	181952	34244	40
Caelo	Water	192421	34765	40
Caelo	Water	20002402	35114	40
Fagron	SyrSpend® SF pH4 aroma free	1704493	33631	40
Caelo	Water	15068701	31675†	15

- 19 156 spectra from a total of 406 batches from further 197 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 825 spectra from 231 *Apo-Ident* customers from 243 batches from the substance/substance group *Water and aqueous solutions*.
- Among them are spectra of independent samples from 235 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	Aloe Vera gel, 1:1	17289003	1
Caelo	Aloe Vera gel, 1:1	19069003	2
Caelo	Aloe Vera gel, 1:1	19255202	1
Caelo	Aloe Vera gel, 1:1	20000289003	1
Caelo	Aloe Vera gel, 1:1	19191401	1
Hedinger	Aloe Vera gel, 1:1	18194304	3
Lamotte	Aloe Vera gel, 1:1	19191403	1
Noweda	Aloe Vera gel, 1:1	17289003	1
Phoenix	Aloe Vera gel, 1:1	17134105	1
Caelo	Aloe vera gel, 10x concentra...	19066601	1
Caelo	Aloe vera gel, 10x concentra...	15185512	1
Fischar	Bepanthen® solution	6317104	1
Liechtenstein	Bepanthen® solution	2300380R	1
Retterspitz/ Phoenix	Retterspitz external	17224	1
Retterspitz/ Phoenix	Retterspitz external	18045	1
Apomix/ Sanacorp	SyrSpend® SF pH4 cherry aroma	15C19/C	1
Bombastus	SyrSpend® SF pH4 cherry aroma	1803724/2	1
Caelo	SyrSpend® SF pH4 cherry aroma	1900093P-190927-2	1
Caelo	SyrSpend® SF pH4 cherry aroma	1806233/2P-190927-3	1
Caelo	SyrSpend® SF pH4 cherry aroma	1507318	3
Caelo	SyrSpend® SF pH4 cherry aroma	1800673/1	2
Caelo	SyrSpend® SF pH4 cherry aroma	1707302/1	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	SyrSpend® SF pH4 cherry aroma	1702015	4
Caelo	SyrSpend® SF pH4 cherry aroma	1803724/2	1
Euro OTC	SyrSpend® SF pH4 cherry aroma	1704492/01	1
Fagron	SyrSpend® SF pH4 cherry aroma	15C19/C	7
Fagron	SyrSpend® SF pH4 cherry aroma	1507318	5
Fagron	SyrSpend® SF pH4 cherry aroma	1503255	19
Fagron	SyrSpend® SF pH4 cherry aroma	1603252/2	11
Fagron	SyrSpend® SF pH4 cherry aroma	1612631	22
Fagron	SyrSpend® SF pH4 cherry aroma	1701543/3	5
Fagron	SyrSpend® SF pH4 cherry aroma	1707302/1	7
Fagron	SyrSpend® SF pH4 cherry aroma	1702015(2Flaschen)	1
Fagron	SyrSpend® SF pH4 cherry aroma	2x1712024	1
Fagron	SyrSpend® SF pH4 cherry aroma	1800673/2	1
Fagron	SyrSpend® SF pH4 cherry aroma	1806233/2	23
Fagron	SyrSpend® SF pH4 cherry aroma	1806233/2P-190618-2	1
Fagron	SyrSpend® SF pH4 cherry aroma	1909423/1	5
Fagron	SyrSpend® SF pH4 cherry aroma	2000326	2
Fagron	SyrSpend® SF pH4 cherry aroma	20004221	1
Fagron	SyrSpend® SF pH4 cherry aroma	1802928	3
Fagron	SyrSpend® SF pH4 cherry aroma	1909673	29
Fagron	SyrSpend® SF pH4 cherry aroma	720023-0003	2
Fagron	SyrSpend® SF pH4 cherry aroma	1800673/1P-180827-1	1
Fagron	SyrSpend® SF pH4 cherry aroma	1803724/2P-180922-1	1
Fagron	SyrSpend® SF pH4 cherry aroma	1806233/2P-190808-3	1
Fagron	SyrSpend® SF pH4 cherry aroma	20000326P-200709-3	1
Fagron	SyrSpend® SF pH4 cherry aroma	518E-07041	1
Fagron	SyrSpend® SF pH4 cherry aroma	1707032/1	1
Fagron	SyrSpend® SF pH4 cherry aroma	1712017	5
Fagron	SyrSpend® SF pH4 cherry aroma	20000326	13
Fagron	SyrSpend® SF pH4 cherry aroma	20004332	1
Fagron	SyrSpend® SF pH4 cherry aroma	4415A-07041	1
Fagron	SyrSpend® SF pH4 cherry aroma	1909423-2	1
Fagron	SyrSpend® SF pH4 cherry aroma	1712024	20
Fagron	SyrSpend® SF pH4 cherry aroma	18062331	1
Fagron	SyrSpend® SF pH4 cherry aroma	1800673	1
Fagron	SyrSpend® SF pH4 cherry aroma	1806233/1	4
Fagron	SyrSpend® SF pH4 cherry aroma	18000673/1	1
Fagron	SyrSpend® SF pH4 cherry aroma	1704992/1	1
Fagron	SyrSpend® SF pH4 cherry aroma	1702015	23
Fagron	SyrSpend® SF pH4 cherry aroma	1803724/2	33
Fagron	SyrSpend® SF pH4 cherry aroma	1900093	18
Fagron	SyrSpend® SF pH4 cherry aroma	180067/1	1
Fargon/AHD	SyrSpend® SF pH4 cherry aroma	1806233/2	1
Fragron	SyrSpend® SF pH4 cherry aroma	1702015	1
Gehe	SyrSpend® SF pH4 cherry aroma	1803724/2	1
Gehe	SyrSpend® SF pH4 cherry aroma	1909673	1
Gehe	SyrSpend® SF pH4 cherry aroma	17122017	1
GEHE	SyrSpend® SF pH4 cherry aroma	1712024	1
GEHE	SyrSpend® SF pH4 cherry aroma	1803724/2	3
GEHE	SyrSpend® SF pH4 cherry aroma	1806233/2	2
Caelo	SyrSpend® SF pH4 cherry aroma	1704492	1
Ichthyol/Gehe	SyrSpend® SF pH4 cherry aroma	1900093	1
Kehr.21.07.2020	SyrSpend® SF pH4 cherry aroma	20000326	1
Caelo	SyrSpend® SF pH4 cherry aroma	1503255	1
PHÖNIX	SyrSpend® SF pH4 cherry aroma	1704492/1	1
Phönix Gotha	SyrSpend® SF pH4 cherry aroma	1909673	1
Phönix Gotha	SyrSpend® SF pH4 cherry aroma	20000326	2
Fagron	SyrSpend® SF pH4 cherry aroma	1800673/1	17
Fagron	SyrSpend® SF pH4 cherry aroma	180623312	1
Caelo	SyrSpend® SF pH4 aroma free	1704493	1

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Supplier	Substance	Batch	Spectra
Caelo	SyrSpend® SF pH4 aroma free	1712023/1	6
Caelo	SyrSpend® SF pH4 aroma free	1812018	1
Caelo	SyrSpend® SF pH4 aroma free	1712023/2	3
Caelo	SyrSpend® SF pH4 aroma free	1712018	1
Fagron	SyrSpend® SF pH4 aroma free	1410D020	7
Fagron	SyrSpend® SF pH4 aroma free	15C12/E	1
Fagron	SyrSpend® SF pH4 aroma free	15C12E	1
Fagron	SyrSpend® SF pH4 aroma free	1706769/1	6
Fagron	SyrSpend® SF pH4 aroma free	1609686	1
Fagron	SyrSpend® SF pH4 aroma free	1706769	1
Fagron	SyrSpend® SF pH4 aroma free	27121704	1
Fagron	SyrSpend® SF pH4 aroma free	1712018	5
Fagron	SyrSpend® SF pH4 aroma free	1712023/2	22
Fagron	SyrSpend® SF pH4 aroma free	18026531	1
Fagron	SyrSpend® SF pH4 aroma free	102653/1	1
Fagron	SyrSpend® SF pH4 aroma free	1802653/4	2
Fagron	SyrSpend® SF pH4 aroma free	1804245/1	23
Fagron	SyrSpend® SF pH4 aroma free	17122018	1
Fagron	SyrSpend® SF pH4 aroma free	1812150/2	10
Fagron	SyrSpend® SF pH4 aroma free	1907122	1
Fagron	SyrSpend® SF pH4 aroma free	190114110	1
Fagron	SyrSpend® SF pH4 aroma free	1802653/1	16
Fagron	SyrSpend® SF pH4 aroma free	1808206/2B	1
Fagron	SyrSpend® SF pH4 aroma free	1808206/2A	1
Fagron	SyrSpend® SF pH4 aroma free	518E-07040	1
Fagron	SyrSpend® SF pH4 aroma free	1704493	11
Fagron	SyrSpend® SF pH4 aroma free	22092008	2
Fagron	SyrSpend® SF pH4 aroma free	22092007	1
Fagron	SyrSpend® SF pH4 aroma free	1808206/2	43
Fagron	SyrSpend® SF pH4 aroma free	1712023/02	1
Fagron	SyrSpend® SF pH4 aroma free	4415A-07040	1
Fagron	SyrSpend® SF pH4 aroma free	1808206/1	3
Fagron	SyrSpend® SF pH4 aroma free	1814231	20
Fagron	SyrSpend® SF pH4 aroma free	1906126	11
Fagron	SyrSpend® SF pH4 aroma free	720024-0003	1
Fagron	SyrSpend® SF pH4 aroma free	1712023/1	3
Fagron	SyrSpend® SF pH4 aroma free	1802653/2	5
Fagron	SyrSpend® SF pH4 aroma free	1802654	6
Fagron	SyrSpend® SF pH4 aroma free	1911010	2
Fagron	SyrSpend® SF pH4 aroma free	1804245/2	2
Fargron/PNACH	SyrSpend® SF pH4 aroma free	1712023/1	1
Fgron / Kehr 03.02.2020	SyrSpend® SF pH4 aroma free	1812150/2	1
Gehe	SyrSpend® SF pH4 aroma free	1804245/1	8
Gehe	SyrSpend® SF pH4 aroma free	1808206/2	5
Gehe	SyrSpend® SF pH4 aroma free	1812150/2	2
Gehe	SyrSpend® SF pH4 aroma free	1814231	3
Herkel B.V./Kehr	SyrSpend® SF pH4 aroma free	1808206/2	1
Kehr.26.03.2020	SyrSpend® SF pH4 aroma free	1814231	1
Caelo	SyrSpend® SF pH4 aroma free	19011410	2
Caelo	SyrSpend® SF pH4 aroma free	1906126	2
Noweda	SyrSpend® SF pH4 aroma free	1712023/2	1
Phönix	SyrSpend® SF pH4 aroma free	1802653/1	1
Phönix	SyrSpend® SF pH4 aroma free	1802653/01	1
Phönix Gotha	SyrSpend® SF pH4 aroma free	1802653/1	2
Phönix Gotha	SyrSpend® SF pH4 aroma free	1802654	4
Sanacorp	SyrSpend® SF pH4 aroma free	19011410	1
Tiofarma B.V.	SyrSpend® SF pH4 aroma free	1410D020	1
Caelo	Water	17145001	3
apomix/ Fiebig	Water	17H24-T09-044709	1
Apotheke	Water	4/20	1

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Supplier	Substance	Batch	Spectra
B.Braun Melsungen AG / ...	Water	18272011	1
B.Braun Melsungen AG / ...	Water	18264014	1
Caelo	Water	15336501	1
Caelo	Water	16211901	1
Caelo	Water	16F13-T16-034297	1
Caelo	Water	16F13-T18-34301	1
Caelo	Water	LOTAP0041	1
Caelo	Water	17114701	2
Caelo	Water	17114801	1
Caelo	Water	17B13-T04-041608	1
Caelo	Water	13121720	1
Caelo	Water	17173001	1
Caelo	Water	17277102	2
Caelo	Water	17282701	3
Caelo	Water	18042901	1
Caelo	Water	18093501	2
Caelo	Water	17295701	1
Caelo	Water	219181	1
Caelo	Water	18109501	1
Caelo	Water	17K27-T16-050588	1
Caelo	Water	18110401	4
Caelo	Water	18E25-T01-056423	1
Caelo	Water	18325001	1
Caelo	Water	18265001	2
Caelo	Water	18J10-01-060845	1
Caelo	Water	19037701	1
Caelo	Water	151005027617	1
Caelo	Water	LOTAP-SP0001	1
Caelo	Water	18G16-T05-058132	1
Caelo	Water	16F13-T11-034264	1
Caelo	Water	20001119001	1
Caelo	Water	18305101	1
Caelo	Water	16353303	1
Caelo	Water	LOTAP0078	1
Caelo	Water	19152801	1
Caelo	Water	17219101	2
Caelo	Water	18E07-T08-055699	1
Caelo	Water	1733981	1
Caelo	Water	17211201	1
Caelo	Water	18178302	3
Caelo	Water	15394201	1
Caelo	Water	16223801	4
Caelo	Water	14IL38	1
Caelo	Water	17K27-T10-050547	1
Caelo	Water	18156401	1
Caelo	Water	18178401	1
Caelo	Water	18263401	1
Caelo	Water	18254801	1
Caelo	Water	18305401	1
Caelo	Water	20002911001	1
Caesar & Loretz GmbH / ...	Water	16127901	1
Caesar & Loretz/Noweda	Water	15394501	1
Chemica GmbH/ Rewe	Water	12345678	1
Dr.Wolff	Water	18061901	1
Fagron	Water	16C22-T09-031414	1
Euro OTC	Water	16F14-T07-034326	1
Fagron	Water	15D13-T09-021469	1
Fagron	Water	16F13-T16-034297	2
Fagron	Water	16F14-T09-034330	1
Fagron	Water	16L12-T11-039624	1

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Supplier	Substance	Batch	Spectra
Fagron	Water	15K10-T04-027614	1
Fagron	Water	16F14-T03-034317	1
Fagron	Water	16L12-T25-039642	2
Fagron	Water	17F23-T06-045760	1
Fagron	Water	17H24-T11-047713	1
Fagron	Water	17E05T11044076	1
Fagron	Water	17E05T07044067	1
Fagron	Water	17K27-T09-050544	2
Fagron	Water	17E05-T13-044080	1
Fagron	Water	18C19-T25	1
Fagron	Water	17K27-T16-050588	1
Fagron	Water	18C19-T31-054017	1
Fagron	Water	15L15-T01-028672	1
Fagron	Water	18E25-T01-056423	1
Fagron	Water	17E05-T03-044051	1
Fagron	Water	17E05-T01-044045	2
Fagron	Water	15H25-T21-025683	1
Fagron	Water	17C31-T05-043064	1
Fagron	Water	16C23-T06-031423	1
Fagron	Water	17H24-T13-047717	1
Fagron	Water	17K27-T15-050585	1
Fagron	Water	18C19-T29-054007	2
Fagron	Water	17L20-T02-051255	1
Fagron	Water	18c13-T14-053737	1
Fagron	Water	18C19T31054017	1
Fagron	Water	18C19-T28-054003	1
Fagron	Water	19A18-T07-063531	2
Fagron	Water	15H25-T14-025670	1
Fagron	Water	16K25-C20-17409	1
Fagron	Water	16L12-T16-039628	1
Fagron	Water	18G16-T04-058129	1
Fagron	Water	16C22-T07-031410	1
Fagron	Water	17L20-T20-0001	1
Fagron	Water	17K27-T11-050552	3
Fagron	Water	15L14-T14-028664	1
Fagron	Water	15L15-T07-028685	1
Fagron	Water	15H25-T18-025678	1
Fagron	Water	17B10-T20-041571	1
Fagron	Water	18C19-T30-054012	2
Fargon/Gehe	Water	19A18-T07-063531	1
Fargon/Kehr	Water	16F13-T18-034301	1
Fargron/Phönix	Water	18C19-T31-054017	1
Fresenius /Noweda	Water	19KK24GA	1
Gehe	Water	17219101	1
GEHE	Water	17114801	1
Caelo	Water	18228801	2
Caelo	Water	18238601	1
Hedinger	Water	219140	1
Hedinger	Water	219208	1
HEDINGER	Water	LOTAP0071	1
HEDINGER	Water	219162	1
Henry Lamotte Oil / Gehe	Water	17K27-T10-050547	1
Caelo	Water	18065601	3
Fagron	Water	18E07-T08-055699	1
L30	Water	17291301	1
Midas	Water	16C22-T07-031410	1
Midas	Water	16L12-T25-039642	1
Fagron	Water	15K10-T08-027626	1
Phoenix	Water	15L14-T14-028664	1
Phoenix	Water	3387	1

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Supplier	Substance	Batch	Spectra
Phönix	Water	18C19-T25-053991	1
Phönix EK:8,37 EUR 2L	Water	17B10-T18-041564	1
Fagron	Water	19A18-T08-063538	1
Sanacorp	Water	18042901	1
Fagron	Water	15D13-T07-021465	1
Walter Schmidt Chemie G…	Water	95058	1
wepa	Water	LOTAP0019	1
wepa	Water	AP00036	1
wepa	Water	LOTAP0034	1
wepa	Water	LOTAP0075	1
Wepa	Water	LOTAP0031	1
Wepa	Water	LOTAP0020	1
Wepa	Water	AP0072	1
Wepa	Water	LOTAP0072	1
Wepa	Water	LOTAP0080	1
Wepa	Water	LOTAP0084	1
Wepa	Water	LOTAP0087	1
WEPA	Water	LOTAP0015	1
WEPA	Water	LOTAP0068	1
WEPA	Water	LOTAP0081	1
Wepa Apothekenbedarf	Water	LOTAP0050	1
WEPA Apothekenbedarf Gm…	Water	LOTAP0095	1
Wepa/ Wepa	Water	LOTAP0077	1
Wepa/AHCA	Water	LOTAP0099	1
WEPA/Krieger	Water	LOTAP0086	1
Wepa/Wepa	Water	LOTAP0037	1
WEPA/WEPA	Water	LOTAP0088	1
Caelo	Aloe vera gel, 10x concentra…	15185503	1
Fagron	SyrSpend® SF pH4 cherry aroma	1503D017	2
Fagron	SyrSpend® SF pH4 cherry aroma	1704492/1	9
Fagron	SyrSpend® SF pH4 aroma free	1412D002	3
Fagron	SyrSpend® SF pH4 aroma free	19011410	7
Fagron	SyrSpend® SF pH4 aroma free	1503D009	3
Caelo	Water		1
kerndl-Noweda	Water		2
Serumwerk Bernburg	Water		1
serumwerk bernburg - Gehe	Water		5

- 7775 spectra from 706 *Apo-Ident* customers from a total of 3304 batches from a further 143 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Water and aqueous solutions* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Water and aqueous solutions* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	1165	0	23 340
Type B	0	1643	2	19 016
Type C	0	810	15	7763

The substance/substance group *Water and aqueous solutions* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9599 %)	100.0000 % (> 99.4850 %)
Type B	100.0000 % (> 99.9455 %)	99.8784 % (> 99.6960 %)
Type C	100.0000 % (> 98.7756 %)	98.1818 % (> 97.8182 %)

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 *Water and aqueous solutions* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Fenistil® Gel	14.52	–
Sebexol® cream lotion pH 5	26.53	–
Sebexol® basic pH 5 formula basis	27.70	–
Wofacutan wash lotion	32.24	–
Hans Karrer Hydrocream MicroSilver	34.79	–
Dimeticone ointment 10% SR	35.30	–
Excipial® U Hydrolotio	40.48	–
Abitima® clinic face cream	46.62	–
Hans Karrer Lipolotion MicroSilver	65.59	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Water and aqueous solutions* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31145	31145	0.00	31.09
31866	31866	0.00	32.67
31880	31880	0.00	33.72
35077	35077	0.00	28.84
31881	31881	0.00	32.49

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Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33430	33430	0.00	25.39
33431	33431	0.00	25.65
35049	35049	0.00	25.92
31623	31623	0.00	31.48
31675	31675	0.00	33.85
32079	32079	0.00	32.82
32785	32785	0.00	19.13
31047	31047	0.00	26.91
31146	31146	0.00	29.69
31857	31857	0.00	26.74
31862	31862	0.00	29.92
33612	33612	0.00	26.32
32313	32313	0.00	29.07
31671	31671	0.00	31.54
31723	31723	0.00	30.02
33787	33787	0.00	29.58
31670	31670	0.00	30.99
34767	34767	0.00	32.47
31722	31722	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 2.3-2021-01

Validated substance/substance group	**Wax ointment (stabilised)**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31111-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Wax ointment (stabilised); Unguentum cereum

Special notes

When selecting the *Wax ointment (stabilised)* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wax ointment (stabilised)	5	8	60

Second-stage model

For differentiation of the substance/substance group *Wax ointment (stabilised)* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Wax ointment (stabilised)*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	Wax ointment (st…	13072102	31111	40	not required
Caelo	Wax ointment (st…	13307701	31167	40	not required
Caelo	Wax ointment (st…	14073701	31444	40	not required
Caelo	Wax ointment (st…	154243	31911	60	20151217*
Caelo	Wax ointment (st…	154244	31912	60	20151217*

Validation samples

A total of 53 906 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 *Wax ointment (stabilised)*. These samples are listed above in the *calibration samples* section. The reference samples come from 5 different batches.
- 24 265 spectra from a total of 499 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Wax ointment (stabilised)*.

*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	Wax ointment (stabilised)	12352501	30967	40
Caelo	Wax ointment (stabilised)	161215	32117	40
Caelo	Wax ointment (stabilised)	161334	32118	40
Caelo	Wax ointment (stabilised)	171714	33550	40
Caelo	Wax ointment (stabilised)	172942	34024	40
Caelo	Wax ointment (stabilised)	191905	34793	40
Caelo	Wax ointment (stabilised)	19000784	34984	40
Caelo	Wax ointment (stabilised)	20002322	35095	40

- 20 481 spectra from a total of 439 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *Apo-Ident* customers carry out the measurements. *HiperScan GmbH* generally does not verify the information provided by the customer regarding manufacturer and batch number.

- 477 spectra from 167 *Apo-Ident* customers from 63 batches from the substance/substance group *Wax ointment (stabilised)*.
- 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	Wax ointment (stabilised)	14073701	1
Alliance Healthcare	Wax ointment (stabilised)	18162202	1
Alliance Healthcare	Wax ointment (stabilised)	19190502	2
Anzag 07.12.12	Wax ointment (stabilised)	12128702	1
Caelo	Wax ointment (stabilised)	1218702	2
Caello/Phönix	Wax ointment (stabilised)	16121501	2
Caelo	Wax ointment (stabilised)	11355202	1
Caelo	Wax ointment (stabilised)	7071204	1
Caelo	Wax ointment (stabilised)	12033602	2
Caelo	Wax ointment (stabilised)	12209401	3
Caelo	Wax ointment (stabilised)	20051012-1	1
Caelo	Wax ointment (stabilised)	1021303	1
Caelo	Wax ointment (stabilised)	12378701	5
Caelo	Wax ointment (stabilised)	U-150513-2	1
Caelo	Wax ointment (stabilised)	12352051	1
Caelo	Wax ointment (stabilised)	11355201	2
Caelo	Wax ointment (stabilised)	20121305	1
Caelo	Wax ointment (stabilised)	14073801	7
Caelo	Wax ointment (stabilised)	140737701	1
Caelo	Wax ointment (stabilised)	1407301	1
Caelo	Wax ointment (stabilised)	140737012	1
Caelo	Wax ointment (stabilised)	15025801	16
Caelo	Wax ointment (stabilised)	28051511	1
Caelo	Wax ointment (stabilised)	14236002	3
Caelo	Wax ointment (stabilised)	15424402	4
Caelo	Wax ointment (stabilised)	16121502	4
Caelo	Wax ointment (stabilised)	16121501	8
Caelo	Wax ointment (stabilised)	16133401	19
Caelo	Wax ointment (stabilised)	1524401	1
Caelo	Wax ointment (stabilised)	17014901	26

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Supplier	Substance	Batch	Spectra
Caelo	Wax ointment (stabilised)	17015002	1
Caelo	Wax ointment (stabilised)	17171401	18
Caelo	Wax ointment (stabilised)	17294202	16
Caelo	Wax ointment (stabilised)	18034602	15
Caelo	Wax ointment (stabilised)	18034601	3
Caelo	Wax ointment (stabilised)	19040001	8
Caelo	Wax ointment (stabilised)	19040002	12
Caelo	Wax ointment (stabilised)	3427	1
Caelo	Wax ointment (stabilised)	12209402	1
Caelo	Wax ointment (stabilised)	14072801	1
Caelo	Wax ointment (stabilised)	15025702	11
Caelo	Wax ointment (stabilised)	13159302	7
Caelo	Wax ointment (stabilised)	19000784002	1
Caelo	Wax ointment (stabilised)	15424401	7
Caelo	Wax ointment (stabilised)	15205402	12
Caelo	Wax ointment (stabilised)	17015001	19
Caelo	Wax ointment (stabilised)	1524301	1
Caelo	Wax ointment (stabilised)	2113Q-03212	1
Caelo	Wax ointment (stabilised)	17294201	17
Caelo	Wax ointment (stabilised)	12033701	4
Caelo	Wax ointment (stabilised)	12352501	4
Caelo	Wax ointment (stabilised)	14235901	13
Caelo	Wax ointment (stabilised)	14236001	3
Caelo	Wax ointment (stabilised)	18162201	3
Caelo	Wax ointment (stabilised)	19190502	2
Caelo	Wax ointment (stabilised)	1114E3212	1
Caelo	Wax ointment (stabilised)	15424301	16
Caelo	Wax ointment (stabilised)	18258501	20
Caelo	Wax ointment (stabilised)	19190501	13
Caelo	Wax ointment (stabilised)	13159303	2
Caelo	Wax ointment (stabilised)	11321302	1
Caeol/Noweda	Wax ointment (stabilised)	17294201	1
Caeol/Phoenix	Wax ointment (stabilised)	15424301	1
Caesar & Loretz GmbH	Wax ointment (stabilised)	13072102	1
Caesar & Loretz GmbH	Wax ointment (stabilised)	18258501	3
Caesar & Loretz GmbH	Wax ointment (stabilised)	18162202	2
Caesar & Loretz GmbH	Wax ointment (stabilised)	19040001	4
Caesar & Loretz GmbH	Wax ointment (stabilised)	19040002	2
Caesar & Loretz GmbH	Wax ointment (stabilised)	19190501	4
Caesar & Loretz GmbH	Wax ointment (stabilised)	19190502	3
Caesar & Loretz GmbH	Wax ointment (stabilised)	19000783001	4
Caesar & Loretz GmbH	Wax ointment (stabilised)	19000784002	1
Caesar & Loretz GmbH/ A...	Wax ointment (stabilised)	19040002	1
Caesar & Loretz GmbH/Ph...	Wax ointment (stabilised)	19040002	1
Caesar & Loretz GmbH/Ph...	Wax ointment (stabilised)	19040001	1
Caesar und Loretz GmbH	Wax ointment (stabilised)	17015001	1
Cealo / Otto Geilenkirc...	Wax ointment (stabilised)	19000783001	1
Cealo/Noweda	Wax ointment (stabilised)	16133401	1
Cealo/Noweda	Wax ointment (stabilised)	19190501	1
Cealo/Sanacorp	Wax ointment (stabilised)	18034602	1
Celo	Wax ointment (stabilised)	15424402	1
Gehe	Wax ointment (stabilised)	13072102	1
Gehe	Wax ointment (stabilised)	16133401	1
GEHE	Wax ointment (stabilised)	17171401	1
Caelo	Wax ointment (stabilised)	18162202	9
Hedinger GmbH &Co KG	Wax ointment (stabilised)	18034602	1
Henry Lamotte Olis GmbH...	Wax ointment (stabilised)	15424301	1
Noweda	Wax ointment (stabilised)	17171401	1
Caelo	Wax ointment (stabilised)	19000783001	5
Caelo	Wax ointment (stabilised)	13307802	13

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Supplier	Substance	Batch	Spectra
Sanacoro W.E:06.03.18 …	Wax ointment (stabilised)	17171401	1
Sanacorp	Wax ointment (stabilised)	12352501	1
Sanacorp	Wax ointment (stabilised)	14073701	1
Sanacorp	Wax ointment (stabilised)	15205402	2
Sanacorp	Wax ointment (stabilised)	17015001	1
Sanacorp	Wax ointment (stabilised)	17294202	1
Sanacorp	Wax ointment (stabilised)	18162202	4
VDL;6,45EUR;21.10.14	Wax ointment (stabilised)	14235901	1
Caelo	Wax ointment (stabilised)	13307701	17
Caelo	Wax ointment (stabilised)	13072102	11
Caelo	Wax ointment (stabilised)	14073701	15

- 8123 spectra from 724 *Apo-Ident* customers from a total of 3483 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Wax ointment (stabilised)* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wax ointment (stabilised)* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 265
Type B	0	320	0	20 481
Type C	0	474	3	8123

The substance/substance group *Wax ointment (stabilised)* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9601 %)	100.0000 % (> 97.5000 %)
Type B	100.0000 % (> 99.9453 %)	100.0000 % (> 98.1250 %)
Type C	100.0000 % (> 98.7849 %)	99.3711 % (> 98.7421 %)

In order to ensure that each substance is entered with the same weight irrespective of the number of spectra available, each spectrum is weighted with the reciprocal value of its number. (If several new spectra of a substance with a very distinctive spectrum are added, the values for *specificity* and *recognition rate* are safer, but are by no means idealised.)

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower the deterioration if the three hypothetical *incorrect results* were added.
Where the number of spectra does not exceed 20, no *recognition rate* is provided.

Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Wax ointment (stabilised)* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Cottonwood ointment	25.95	–
Neribas® fat ointment	26.48	–
Marjoram ointment	27.19	–
Protegin® XN	32.27	–
Excipial® almond oil ointment	37.50	–
Balm Bio Nature	37.87	–
Salicylic white paraffin 10%	42.43	–
White paraffin oil	43.32	–
Argan oil	44.46	–
Deumavan® protection ointment neutral	62.60	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wax ointment (stabilised)* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31111	31111	0.00	36.32
31167	31167	0.00	38.76
31444	31444	0.00	35.71
31911	31911	0.00	31.94
31912	31912	0.00	39.25

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 2.3-2021-01

Validated substance/substance group	**White paraffin oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	32342-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

White paraffin oil; Oleum Vaselini album

Special notes

When selecting the *White paraffin oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
White paraffin oil	2	1	6

Second-stage model

For differentiation of the substance/substance group *White paraffin oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *White paraffin oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Caelo	White paraffin oil	162192	32342	40	20160729*
Caelo	White paraffin oil	15380806	32565	40	not required

Validation samples

A total of 53 906 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 *White paraffin oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *White paraffin oil*.
- 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	White paraffin oil	14338604	32454	40
Caelo	White paraffin oil	14338604	32846	40

- 20 721 spectra from a total of 446 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 8 *Apo-Ident* customers from 6 batches from the substance/substance group *White paraffin oil*.
- 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	White paraffin oil	18226101	1
Caelo	White paraffin oil	18226105	1
Caelo	White paraffin oil	17175501	1
Caelo	White paraffin oil	17175506	1
Caelo	White paraffin oil	17175509	1
Caesar & Loretz GmbH	White paraffin oil	17175509	1
Caesar & Loretz GmbH/No…	White paraffin oil	18226105	1
Cealo / Spangro	White paraffin oil	16219204	1

- 8592 spectra from 735 *Apo-Ident* customers from a total of 3540 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *White paraffin oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *White paraffin oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	80	0	20 721
Type C	0	8	0	8592

The substance/substance group *White paraffin oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9456 %)	100.0000 % (> 92.5000 %)
Type C	100.0000 % (> 98.7929 %)	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 *White paraffin oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Deumavan® protection ointment neutral	13.34	–
Neribas® fat ointment	21.17	–
Cottonwood ointment	24.52	–
Marjoram ointment	25.63	–
Protegin® XN	25.70	–
Asche Basis® fat ointment	27.45	–
Wax ointment (stabilised)	43.94	–
Lygal® head ointment N 3%	44.21	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *White paraffin oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
32342	32342	0.00	14.94
32565	32565	0.00	17.17

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 2.3-2021-01

Validated substance/substance group	**Wintergreen oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	30455-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Wintergreen oil; Oleum gaultheria procumbens

Special notes

When selecting the *Wintergreen oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.

2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.

3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Wintergreen oil	2	2	10

Second-stage model

For differentiation of the substance/substance group *Wintergreen oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Wintergreen oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Taoasis	Wintergreen oil	5411006-117696	31543	56	not required
Taoasis	Wintergreen oil	1828-125286	32807	40	not required

Validation samples

A total of 53 906 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

Type A All calibration spectra.

- 96 spectra of 2 reference samples from the substance/substance group *Wintergreen oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 409 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Wintergreen oil*.
- 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
Primavera	Wintergreen oil	00129A27	34399	40
Taoasis	Wintergreen oil	1953-128607	33624	40
Taoasis	Wintergreen oil	1828-125286	32936	40
Taoasis	Wintergreen oil	1953-128607	33625	40

- 20 641 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 11 batches from the substance/substance group *Wintergreen oil*.

- 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	Wintergreen oil	10318703	1
Caelo	Wintergreen oil	10318714	1
Caelo	Wintergreen oil	13099205	1
Caelo	Wintergreen oil	15087406	1
Caelo	Wintergreen oil	13099202	1
Taoasis	Wintergreen oil	423121-90971	1
Taoasis	Wintergreen oil	97540	1
Taoasis	Wintergreen oil	1303-121125	1
Taoasis	Wintergreen oil	2170-291	1
Taoasis/Taoasis	Wintergreen oil	2387-7212	1
Taoasis	Wintergreen oil		1

- 8589 spectra from 736 *Apo-Ident* customers from a total of 3535 batches from a further 149 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Wintergreen oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Wintergreen oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive*/*negative*) and the validation spectrum type ($A/B/C$).

	False positive	True positive	False negative	True negative
Type A	0	96	0	24 409
Type B	0	159	1	20 641
Type C	0	10	1	8589

The substance/substance group *Wintergreen oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9605 %)	100.0000 % (> 93.7500 %)
Type B	100.0000 % (> 99.9454 %)	99.3750 % (> 97.5000 %)
Type C	100.0000 % (> 98.7907 %)	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 *Wintergreen oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clove oil	274.25	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Wintergreen oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
31543	31543	0.00	294.26
32807	32807	0.00	295.27

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 2.3-2021-01

Validated substance/substance group	**Yarrow oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	33795-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Yarrow oil

Special notes

When selecting the *Yarrow oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Yarrow oil	2	3	0

Second-stage model

For differentiation of the substance/substance group *Yarrow oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Yarrow oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Yarrow oil	00516E25	33795	40	not required
Taoasis	Yarrow oil	2041-316	33822	40	not required

Validation samples

A total of 53 906 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 *Yarrow oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 2 different batches.
- 24 425 spectra from a total of 502 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Yarrow oil*.
- 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
Primavera	Yarrow oil	00677E26	34174	40
Primavera	Yarrow oil	00197J26	34295	40
Taoasis	Yarrow oil	128700	33823	40

- 20 681 spectra from a total of 444 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Yarrow oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Yarrow oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Yarrow oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 425
Type B	0	107	13	20 681
Type C	0	0	0	8600

The substance/substance group *Yarrow oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9606 %)	100.0000 % (> 92.5000 %)
Type B	100.0000 % (> 99.9455 %)	89.1667 % (> 86.6667 %)
Type C	100.0000 % (> 98.8097 %)	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 *Yarrow oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Citus oil	20.69	–
Myrtle oil	21.81	–
Hyssop oil	24.97	–
Marjoram oil	27.58	–
Angelica root oil	33.64	–
Spearmint oil	41.60	–
Ravensara oil	41.87	–
Juniper oil	43.80	–
Cypress oil	46.53	–
Dwarf pine oil	47.16	–
Sage oil	49.25	–
Matricaria oil, morrocan	49.75	–
Niaouli oil	50.07	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Yarrow oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
33795	33795	0.00	52.15
33822	33822	0.00	21.04

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 2.3-2021-01

Validated substance/substance group	**Ylang-ylang oil**
Substance class	APIs & excipients, liquid/semi-solid (other)
Report date	22/03/2021
Report number	31506-2021-03-22
Executing company	HiperScan GmbH Weißeritzstraße 3 01067 Dresden Germany

Relevant substance names

Ylang-ylang oil; Oleum ylang-ylang

Special notes

When selecting the *Ylang-ylang oil* substance/substance group, the following information is displayed to the user:

no information

Applicable documents

978-3-7692-7517-9	*European Pharmacopoeia 10th Edition, Basic Version 2020* [3]
Komm2.2.40	*Erfüllung von* Ph. Eur. 2.2.40 *durch* Apo-Ident [4]
AA004	*Erstellung und Validierung eines IdentModul-Updates*

Validation method

Validation is performed after every change to the chemometric model (also "database") in three steps:

1. The chemometric model is calculated from the calibration spectra using a *PCA algorithm*. The calibration spectra originate from the calibration samples of all substances in this class.
2. In the *chemometric model* generated, the distances between all separable substances are checked for compliance with the specified safety distances.
3. All spectra are presented to the generated chemometric model for evaluation. In three runs, the reference spectra (*Type A*), spectra from independent samples (*Type B*), and spectra from the field (*Type C*) are presented successively. Here, no single *false positive* result is permitted.

Finally, a report is generated from the validation run results and is archived together with the parameters of the model generation in audit-compliant manner.

Number of independent samples (batches) in calibration and validation

A sample is considered independent if no sample from the same batch has been included in the calibration of the chemometric model.

Substance	Type A	Type B	Type C
Ylang-ylang oil	4	2	0

Second-stage model

For differentiation of the substance/substance group *Ylang-ylang oil* the following second-stage model is used:

no second-stage model

Calibration samples

Only spectra which have been recorded by *HiperScan GmbH* from traceable samples are used for the generation of the chemometric models. The following samples have been obtained from the substance/substance group *Ylang-ylang oil*:

Supplier	Substance	Batch	Sample ID	Spectra	Certificate
Primavera	Ylang-ylang oil	00403M26	34382	40	not required
Taoasis	Ylang-ylang oil	140114-115612	31506	60	not required
Taoasis	Ylang-ylang oil	07122-119828	31653	60	not required
Taoasis	Ylang-ylang oil	41813-124965	32808	40	not required

Validation samples

A total of 53 906 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 *Ylang-ylang oil*. These samples are listed above in the *calibration samples* section. The reference samples come from 4 different batches.
- 24 305 spectra from a total of 500 batches from further 160 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix A*. The samples in *Appendix A* were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

Type B Spectra from independent samples not included in the database structure. Measurement is carried out by *HiperScan GmbH*.

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a †. The following applies to the remaining unmarked samples: In the same batch, there 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 *Ylang-ylang oil*.
- 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
Taoasis	Ylang-ylang oil	43197-126348	33049	40
Taoasis	Ylang-ylang oil	B966015-128199	33648	40

- 20 721 spectra from a total of 445 batches from further 203 substances. These spectra were recorded by *HiperScan GmbH*. *Type B* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type B* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix B*.

Type C Spectra of independent samples not included in the database structure. *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 *Ylang-ylang oil*.

- 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.

- 8600 spectra from 736 *Apo-Ident* customers from a total of 3546 batches from a further 150 substances. These spectra were recorded by *Apo-Ident* customers. *Type C* samples are documented within this entire report. If the substance can be identified with this chemometric model, the samples are listed in the *Type C* section of each substance page. If the substance cannot be identified by this model, the samples are listed in *Appendix C*.

Validation results

The validation runs checked whether the substance/substance group *Ylang-ylang oil* can clearly be distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *Ylang-ylang oil* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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	24 305
Type B	0	34	46	20 721
Type C	0	0	0	8600

The substance/substance group *Ylang-ylang oil* can be clearly distinguished from all other substances. In order to make these figures comparable, the weighted *true negative rate* (*specificity*) and the weighted *true positive rate* (*recognition rate*) are determined:

	Specificity	Recognition rate
Type A	100.0000 % (> 99.9602 %)	100.0000 % (> 97.0000 %)
Type B	100.0000 % (> 99.9456 %)	42.5000 % (> 38.7500 %)
Type C	100.0000 % (> 98.8097 %)	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 *Ylang-ylang oil* in the substance class *APIs & excipients, liquid/semi-solid (other)*. Furthermore, their *Mahalanobis distance* is specified within the main model and, where appropriate, within the second-stage model.

Substance	Distance in main model	Distance in second-stage model
Clary sage oil	37.90	–
Petitgrain oil	48.75	–
Lavender oil	61.59	–

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Ylang-ylang oil* is separated from critical neighbours in a second-stage model, all the remaining substances in the second-stage model follow.

Identity according to identity test using NIR spectroscopy

For each substance, a certificate of the correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance:

Sample ID	Reference sample ID	Distance to reference sample	Distance to next foreign sample
34382	34382	0.00	68.87
32808	32808	0.00	74.56
31506	31506	0.00	86.88
31653	31653	0.00	35.35

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.

Appendix A: Additional calibration samples (*Type A*)

Not required.

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 79 batches. From these 3410 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
Actavis	Abitima® clinic body lotion	145054	40	not required
Actavis	Abitima® clinic body lotion	159997	40	not required
Actavis	Abitima® clinic body lotion	159997	40	not required
Dr. Wolff	Anefug® Simplex	234280	40	not required
Dr. Wolff	Anefug® Simplex	237590	40	1407216
Primavera	Anise seed oil	00480L26	40	not required
Taoasis	Black cumin oil	504511-115611	40	not required
Koko	dermaviduals® base gel	L003L13	60	not required
Allergika	Dermifant® kids lotion	1301020	80	not required
Allergika	Dermifant® kids lotion	1306020	40	not required
Allergika	Dermifant® kids lotion	1607080	40	not required
Allergika	Dermifant® kids lotion	1705081	40	not required
Primavera	Douglas fir oil	00539M26	40	not required
Fagron	Fitalite™	14B18-T01-010352	60	not required
Fagron	Fitalite™	14B18-T01-010352	60	not required
Fagron	Fitalite™	1503259	40	not required
Fagron	Fitalite™	1503259	40	not required
Fagron	Fitalite™	1503259	40	not required
Pharmapol	Glycerol trinitrate 5%	228718	40	not required
Pharmapol	Glycerol trinitrate 5%	232961	60	not required
Primavera	Ho leaf oil	00388M26	40	not required
Primavera	Jasmine 4% in alcohol	00184A27	40	not required
Spirig Pharma	Kerasal® base ointment	M031	40	not required
Spirig Pharma	Kerasal® base ointment	N011	40	not required
Primavera	Lavandin oil	00508L26	40	not required
Primavera	Lemon verbena leaf oil	00540M26	40	not required
Dr. Wolff	Linola® acute 0.5%	334620	40	not required
Dr. Wolff	Linola® sun protection SPF 50 lotion	134530	40	not required
Primavera	Litsea oil	00496L26	40	not required
Caelo	Milking grease Special without Osmaron®	162049	40	20160711*
Paddock	Ora-Blend®	2280130	40	not required
Perrigo	Ora-Blend® SF	3112578	40	not required
Fagron	Ora-Plus®	3334081	60	not required
Perrigo	Ora-Plus®	3334081	40	not required
Fagron	Ora-Sweet®	3062252	40	not required
Perrigo	Ora-Sweet®	3062252	40	not required
Stiefel	Physiogel® hypoallergenic cream	343P	40	not required
Stiefel	Physiogel® hypoallergenic cream	6940	40	not required
Caelo	Pine oil rubbing alcohol	162091	40	20160713*
Stoko	Praecutan® lotion F	0915777806	40	not required
Stoko	Praecutan® lotion F	011657101571	40	not required
Einhorn-Apoth...	Rizol raw material	AL0413-1	60	not required
Primavera	Rose oil 10%	00721716	40	not required
Primavera	Rose oil, pure	00099L26	40	not required

continued on the next page

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Supplier	Substance	Batch	Spectra	Certificate
Taoasis	Rose oil, pure	12014-120330H08	40	not required
Salderman Gmb…	Salderman base emulsion	180123	40	not required
Primavera	Seabuckthorn oil, organic	00346E26	40	not required
Primavera	Spanish sage oil	00057G26	40	not required
Bene	Thrombocid® gel	401B101	40	not required
Bene	Thrombocid® gel	401B101	40	not required
Bene	Thrombocid® gel	403I143	40	not required
Bene	Thrombocid® gel	403I143	40	not required
Bene	Thrombocid® gel	403I143	40	not required
Bene	Thrombocid® ointment	410B113	40	not required
Bene	Thrombocid® ointment	410B113	40	not required
Bene	Thrombocid® ointment	408C141	40	not required
Bene	Thrombocid® ointment	409A151	40	not required
Taoasis	Tolu res. 50% oil	493887-105383BAC90451	40	not required
Primavera	Tolu Resinoid	00115A25	40	not required
Taoasis	Tonka extract	3636K08	40	not required
Bayer	Ultrabas®	33851A	40	not required
Hecht Pharma …	Ultrabas®	34069	40	not required
Bayer	Ultraphil®	22100A	40	not required
Bayer	Ultrasicc®	33614A	40	not required
Hecht Pharma …	Ultrasicc®	34837	40	not required
Caelo	Ultrasound contact gel	12031301	40	not required
Taoasis	Vanilla extract oil	789171-114788	40	not required
Caelo	Vario base cream	12077902	50	1405329
Caelo	Vario base cream	13257102	40	1405330
Fagron	Versatile™	14B19-T02-010391	60	not required
Fagron	Versatile™	14B19-T02-010391	60	not required
Fagron	Versatile™	1503256	40	not required
Fagron	Versatile™	1503256	40	not required
Fagron	Versatile™	1503256	40	not required
Fagron	Versatile™ Rich	14B19-T08-010395	60	not required
Fagron	Versatile™ Rich	14B19-T04-010395	60	not required
Fagron	Versatile™ Rich	1503257	40	not required
Fagron	Versatile™ Rich	1503257	40	not required
Fagron	Versatile™ Rich	1503257	40	not required

*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 86 batches. From these, 145 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
Dr. Wolff	Anefug® Simplex	136840	1
Anzag	Capsaicin liquid extr...	120503801	1
Euro OTC	Capsaicin liquid extr...	6061204	1
Euro OTC	Capsaicin liquid extr...	12111205	1
Euro OTC	Capsaicin liquid extr...	1201010-01	1
Euro OTC	Capsaicin liquid extr...	1205038-01	2
EUro/AHD	Capsaicin liquid extr...	1205038-02	1
Allergika/Kehr	Dermifant® kids lotion	1604060	1
Sanacorp EK:10,80 ...	Dermifant® kids lotion	1705111	1
Fagron	Fitalite™	1503259	2
Gehe	Glycerol trinitrate 5%	214895	1
Gehe	Glycerol trinitrate 5%	221414	3
Pharmapohl	Glycerol trinitrate 5%	18102013A	1
Pharmapol	Glycerol trinitrate 5%	219108	4
Pharmapol	Glycerol trinitrate 5%	224310	5
Pharmapol	Glycerol trinitrate 5%	224310(ex)224658(in)	1
Pharmapol	Glycerol trinitrate 5%	226578	10
Pharmapol	Glycerol trinitrate 5%	228718	11
Pharmapol	Glycerol trinitrate 5%	2504130l	1
Pharmapol	Glycerol trinitrate 5%	AKD81	1
Pharmapol	Glycerol trinitrate 5%	232961	3
Pharmapol	Glycerol trinitrate 5%	234783	2
Pharmapol Arzneimitte...	Glycerol trinitrate 5%	232961	6
Pharmapol/Zentrum Apo	Glycerol trinitrate 5%	2913A-07002	1
Anzag/Galderma	Kerasal® base ointment	S075	1
Galderma/Gehe	Kerasal® base ointment	S061	1
Galdermna/Anzag	Kerasal® base ointment	S041	4
Spirig	Kerasal® base ointment	LOTRO12	1
Spirig Pharma	Kerasal® base ointment	N021	1
Spirig/Gehe	Kerasal® base ointment	S076	1
Spirig/Sanacorp	Kerasal® base ointment	N011	1
Caelo	Milk Cordes® O/W Emul...	13D001	2
Ichthyol	Milk Cordes® O/W Emul...	60613	1
Ichthyol - Gesellschaft	Milk Cordes® O/W Emul...	11D037	1
Ichthyol / Noweda	Milk Cordes® O/W Emul...	12D008	5
IchthyolGmbH/Anzag	Milk Cordes® O/W Emul...	12D003	2
Ichtyol, Noweda	Milk Cordes® O/W Emul...	13d007	1
Fagron	Ora-Blend® SF	3745164	1
Fagron	Ora-Blend® SF	4136370	1
Gehe	Ora-Blend® SF	2038178	1
Gehe	Ora-Blend® SF	3112578	1
Perrigo	Ora-Blend® SF	2088609	1
Phönix	Ora-Blend® SF	3434856	2
Phönix	Ora-Blend® SF	3475164	1
Fagron	Ora-Sweet®	3414679	1
Fagron	Ora-Sweet®	4247427	2
GSK Stiefel	Physiogel® hypoallerg...	859R	1

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Supplier	Substance	Batch	Spectra
GSK/Stiefel	Physiogel® hypoallerg...	538T	1
PHOENIX 21.10.2013	Physiogel® hypoallerg...	1142N	1
Phoenix/Stiefel	Physiogel® hypoallerg...	399P	1
Stiefel	Physiogel® hypoallerg...	926Q	1
Stiefel	Physiogel® hypoallerg...	270T	1
Stiefel	Physiogel® hypoallerg...	537T	1
Stiefel/Noweda	Physiogel® hypoallerg...	163R	1
Stiefel/Sanacorp	Physiogel® hypoallerg...	10000	1
Dyckerhoff	Regeneresen	60611dü-2	1
Dyckerhoff	Regeneresen	150173th-2	1
Dyckerhoff	Regeneresen	120292Ov-2	1
Dyckerhoff	Regeneresen	120323Lu-2	1
Dyckerhoff	Regeneresen	120313Kn-2	1
Dyckerhoff	Regeneresen	1503839-Na	1
Dyckerhoff	Regeneresen	120333NN-2	1
Dyckerhoff	Regeneresen	120053NNR-2	1
Arkeo Immun UG	Rizol raw material	1192HJ	2
Caelo	Rizol raw material	15144304	1
Steidl/Phytolab	Rizol raw material	200812174102290	1
Taoasis	Tolu res. 50% oil	493887-105384	1
Taoasis	Tolu res. 50% oil	546022-114802	2
Taoasis	Tolu res. 50% oil	546022-122636	1
Taoasis	Tolu res. 50% oil	23772-118646	1
Taoasis	Tolu res. 50% oil	23772-119167	1
Caelo	Vario base cream	13143401	1
Caelo	Vario base cream	14331902	4
Caelo	Vario base cream	16032402	1
Caelo	Vario base cream	13257102	2
Caelo	Vario base cream	12077902	1
Bombastus	Vario base cream	12375801	1
Phoenix 30.1.2013	Vario base cream	12172501	1
Fagron	Versatile™	1503256	1
Fagron	Versatile™	14B19-T02-010391	2
Fagron	Versatile™ Rich	247224-0002	1
Fagron	Versatile™ Rich	14B19-T04-0130395	1
Fagron	Versatile™ Rich	1503257	4
Phönix	Versatile™ Rich	1503258	1
Taoasis	Wild rose oil	99149-99474	1
Taoasis	Wild rose oil	106177-106175	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).

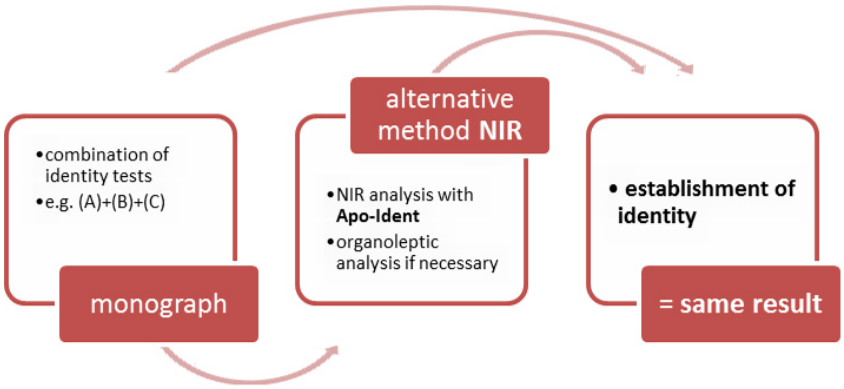

Figure 2: The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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].

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