

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

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## Introduction

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

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

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

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

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

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

## Context of this document

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

- *NIR spectroscopy as a method for identity testing*: The *Ph. Eur.* [3] describes NIR spectroscopy in *Section 2.2.40* as an analytical method which is also suitable for the identification of raw materials. Therefore, validation of the method as such is not necessary.
- *Performance of the instrument*: The *Ph. Eur.* [3] furthermore describes the apparatus and the testing of its performance in *Section 2.2.40*. The document *Erfüllung von 2.2.40 Ph. Eur. durch Apo-Ident* [4] compares the implementation by *Apo-Ident* with this monograph in order to prove that *Apo-Ident* meets the specifications of the Pharmacopoeia. Each individual instrument delivered to a pharmacy is qualified in accordance with the tests described in “*Control of Instrument Performance*”. In this test, the unit consisting of analysis instrument hardware and the *QuickStep* spectroscopy software is assessed. The result is documented in a test protocol which is kept at the pharmacy.
- *Validation of the database* is documented separately for each substance class. The report at hand documents the substance class *APIs & excipients, 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. Bezugsquellen-nachweis für Rezepturbestandteile* [Sources of supply for compounding] [7]).
- b) Testing the suitability according to *ApBetrO* [Pharmacies Rules and Regulations] §§ 6, 11, that is to say the availability of a valid manufacturer certificates via identity, purity and contents of the batch.
- c) Recording standard 40 spectra of the sample in different positions, as a standard on four instruments. Here, handling and presentation of the samples as later in the pharmacy.
- d) Visual checking for anomalies in the spectra. In case of indications of measurement errors, measurement must be repeated. If a signature is missing in the spectrum, the substance may be excluded from the start as not promising (the spectra are nonetheless entered in the database validation as independent *Type B* spectra).
- e) Testing identity. For each substance, a certificate of correct identity is obtained from an independent GMP-certified test laboratory. If the identity of the sample can be provided using NIR on an independently tested reference sample, in the respective following substance page of this validation documentation the *Mahalanobis distance* to this reference sample is specified as well as the *Mahalanobis distance* to the next non-identical substance. Such samples underline the statistical spread of the original reference substance, but cannot add any new characteristics of the substance.

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

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

## 2. Generating the chemometric models (calibration)

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

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

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

### 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 themselves and keeps the test certificates.

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

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

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

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

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

## Significance of testing with *Apo-Ident*

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

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

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

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

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

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

## Conclusion

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



## Explanation of terminology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

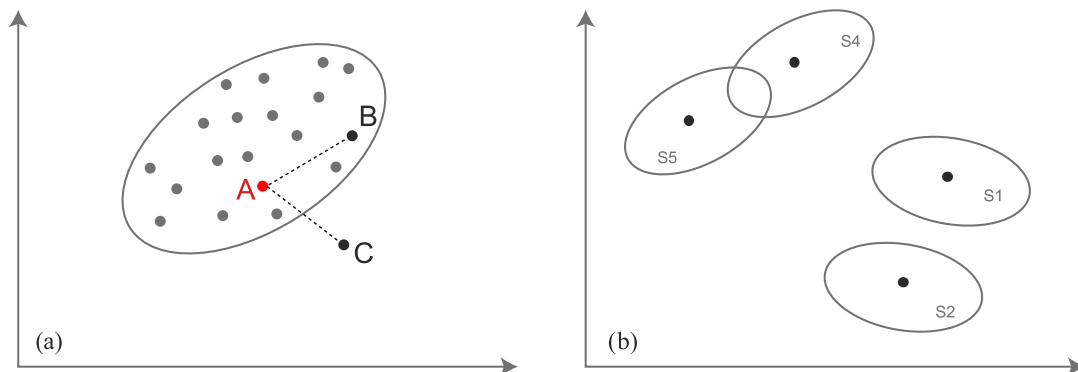


**Figure 1:** (a) The *Mahalanobis distance* from *A* to *B* is less than from *A* to *C*. However, the Euclidean distances are identical. (b) The *Mahalanobis distance* between the two measurement series *S4* and *S5* is smaller than between *S1* and *S2*. However, the Euclidean distances are identical.

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



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

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

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

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

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

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

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



## Summary

A total of 54961 spectra from 4521 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        | 512     | 24 705  |

From category *A* a total of 24 705 spectra from 512 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        | 451     | 20 961  |

From category *B* a total of 20 961 spectra from 451 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        | 3743    | 9295    |

From category *C* a total of 9295 spectra from 3743 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              | 24 705        | 0              | 2 421 090     |
| Type B | 0              | 16 450        | 1101           | 2 056 435     |
| Type C | 0              | 8810          | 340            | 911 016       |

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 85 %) |
| Typ B | 100.000 00 % (> 99.999 45 %) | 92.040 60 % (> 92.008 79 %)  |
| Typ C | 100.000 00 % (> 99.988 00 %) | 93.677 38 % (> 93.023 94 %)  |

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

In order to illustrate the impact of the number of spectra, a comparison is made in parentheses as to how the *specificity* or *recognition rate* would worsen if three additional incorrect results were to exist amongst the spectra (*Rule of Three* [10, 11]). The larger the number of spectra, the lower 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 2.4-2021-02

Validated substance/substance group **Alfason Basis Cresa<sup>®</sup>**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30723-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Alfason Basis Cresa<sup>®</sup>

### Special notes

When selecting the *Alfason Basis Cresa<sup>®</sup>* 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/substance group        | Type A | Type B | Type C |
|----------------------------------|--------|--------|--------|
| Alfason Basis Cresa <sup>®</sup> | 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 54 961 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.
- 24 511 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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® | 14c32-78          | 1       |
| Astellas                   | Alfason Basis Cresa® | 14J02/77          | 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® | 15H06/80          | 1       |
| Astellas Pharma            | Alfason Basis Cresa® | 16A06/76          | 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® | 17017/76          | 1       |
| Caelo                      | Alfason Basis Cresa® | 17EB2/75          | 3       |
| 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® | 18D20/75 (3x350g) | 1       |
| Leo Pharma/Gehe            | Alfason Basis Cresa® | 18A29/75          | 1       |

*continued on the next page*

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

- 9225 spectra from 770 *Apo-Ident* customers from a total of 3633 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<sup>®</sup>* can clearly be 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<sup>®</sup>* and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to the expected result (*positive/negative*) and the validation spectrum type (*A/B/C*).

|               | False positive | True positive | False negative | True negative |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 194           | 0              | 24 511        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 69            | 1              | 9225          |

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

|               | Specificity              | Recognition rate         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.9072 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7988 %) | 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*<sup>®</sup> 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<br>main model | Distance in<br>second-stage model |
|--------------------------------------------|---------------------------|-----------------------------------|
| Alfason <sup>®</sup> Repair                | 13.96                     | —                                 |
| Linola <sup>®</sup> H fat N                | 17.35                     | —                                 |
| Linola <sup>®</sup> fat cream              | 18.06                     | —                                 |
| Neribas <sup>®</sup> ointment              | 25.59                     | —                                 |
| Asche Basis <sup>®</sup> ointment          | 33.35                     | —                                 |
| Dermatop <sup>®</sup> base ointment        | 35.24                     | —                                 |
| Bepanthen <sup>®</sup> Wund- und Heilsalbe | 40.30                     | —                                 |
| Excipial <sup>®</sup> lipo cream           | 74.20                     | —                                 |

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

### Identity according to identity test using NIR spectroscopy

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

| Sample ID | Reference<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30723     | 30723                  | 0.00                            | 20.47                              |
| 31071     | 31071                  | 0.00                            | 18.94                              |
| 32064     | 32064                  | 0.00                            | 23.94                              |
| 32815     | 32815                  | 0.00                            | 17.19                              |

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 2.4-2021-02

|                                     |                                                                              |
|-------------------------------------|------------------------------------------------------------------------------|
| Validated substance/substance group | Allergika evening primrose oil cream 20% / Dermifant <sup>®</sup> kids cream |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                                 |
| Report date                         | 11/06/2021                                                                   |
| Report number                       | 30970-2021-06-11                                                             |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany              |

### Relevant substance names

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

### Special notes

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

*no information*

### Applicable documents

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

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group                                                       | Type A | Type B | Type C |
|---------------------------------------------------------------------------------|--------|--------|--------|
| Allergika evening primrose oil cream 20% /<br>Dermifant <sup>®</sup> kids cream | 6      | 4      | 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 54 961 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.
- 24 385 spectra from a total of 503 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 447 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       |

- 9279 spectra from 772 *Apo-Ident* customers from a total of 3664 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 320           | 0              | 24 385        |
| <b>Type B</b> | 0              | 160           | 0              | 20 801        |
| <b>Type C</b> | 0              | 16            | 0              | 9279          |

The substance/substance group *Allergika evening primrose oil cream 20% / Dermifant<sup>®</sup> 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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9602 %) | 100.0000 % (> 98.1250 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 96.2500 %) |
| <b>Type C</b> | 100.0000 % (> 98.8020 %) | 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<sup>®</sup> 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.

| <b>Substance</b>                               | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|------------------------------------------------|-------------------------------|---------------------------------------|
| Excipial <sup>®</sup> U Lipolotio              | 13.30                         | —                                     |
| Lipoderm <sup>®</sup> lotion                   | 21.38                         | —                                     |
| DMS <sup>®</sup> base cream high classic       | 21.60                         | —                                     |
| Dermatest base ointment                        | 21.83                         | —                                     |
| Lipolotio urea 5% F body lotion                | 23.54                         | —                                     |
| DMS <sup>®</sup> base cream high classic plus  | 26.51                         | —                                     |
| Abitima <sup>®</sup> clinic body cream         | 30.42                         | —                                     |
| Neuroderm <sup>®</sup> moisturising cream lipo | 36.09                         | —                                     |
| Excipial <sup>®</sup> U10 Lipolotio            | 39.09                         | —                                     |
| Neuroderm <sup>®</sup> moisturising cream      | 43.29                         | —                                     |
| Eucerinum W/O basis                            | 43.55                         | —                                     |
| DMS <sup>®</sup> base cream classic            | 47.67                         | —                                     |
| Hans Karrer Lipocream MicroSilver              | 49.67                         | —                                     |
| Fabitol <sup>®</sup> base cream                | 64.11                         | —                                     |

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<sup>®</sup> 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                         | 17.40                           |
| 31062     | 31062               | 0.00                         | 20.98                           |
| 31725     | 31725               | 0.00                         | 19.10                           |
| 31871     | 31871               | 0.00                         | 17.63                           |
| 33486     | 33486               | 0.00                         | 17.99                           |
| 33639     | 33639               | 0.00                         | 18.37                           |

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





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **alpha-bisabolol (racemic) at least 85%**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31464-2021-06-11  
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/substance group              | Type A | Type B | Type C |
|----------------------------------------|--------|--------|--------|
| alpha-bisabolol (racemic) at least 85% | 1      | 3      | 8      |

## 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 54 961 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.
- 24 585 spectra from a total of 508 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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.

- 10 spectra from 7 *Apo-Ident* customers from 8 batches from the substance/substance group *alpha-bisabolol (racemic) at least 85%*.
- Among them are spectra of independent samples from 8 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier             | Substance                       | Batch       | Spectra |
|----------------------|---------------------------------|-------------|---------|
| Caelo                | 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       |
| Caesar & Loretz GmbH | alpha-bisabolol (racemic) at... | 19000485002 | 1       |
| Spangro 28.01.2019   | alpha-bisabolol (racemic) at... | 18058506    | 1       |
| Spangro 28.1.2019    | alpha-bisabolol (racemic) at... | 180580506   | 1       |

- 9285 spectra from 772 *Apo-Ident* customers from a total of 3667 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 24 585        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 10            | 0              | 9285          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8044 %) | 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Citronella oil | 49.18                     | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31464     | 31464                  | 0.00                            | 50.82                              |
| 31465     | 31465                  | 0.00                            | 50.69                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Angelica root oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30535-2021-06-11  
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/substance group | 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 54 961 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.
- 24 465 spectra from a total of 504 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 20      |

- 20 861 spectra from a total of 448 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 | 32229229-1384      | 1       |
| Taoasis  | Angelica root oil | 1049239-3525       | 1       |
| Taoasis  | Angelica root oil | 129271             | 1       |

- 9288 spectra from 772 *Apo-Ident* customers from a total of 3668 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 24 465        |
| <b>Type B</b> | 0              | 80            | 20             | 20 861        |
| <b>Type C</b> | 0              | 6             | 1              | 9288          |

<sup>†</sup>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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9603 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 80.0000 % (> 77.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8072 %) | 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.

| <b>Substance</b>  | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|-------------------|-------------------------------|---------------------------------------|
| Dwarf pine oil    | 14.03                         | —                                     |
| Spearmint oil     | 24.98                         | —                                     |
| Frankincense oil  | 26.66                         | —                                     |
| Swiss pine oil    | 29.74                         | —                                     |
| Marjoram oil      | 31.56                         | —                                     |
| Silver fir oil    | 38.26                         | —                                     |
| Spruce needle oil | 38.51                         | —                                     |
| Citrus oil        | 41.63                         | —                                     |
| Juniper oil       | 42.48                         | —                                     |
| Cumin oil         | 44.34                         | —                                     |
| Camphor oil       | 44.36                         | —                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 30964            | 30964                      | 0.00                                | 30.29                                  |
| 31682            | 31682                      | 0.00                                | 26.66                                  |
| 31780            | 31780                      | 0.00                                | 31.57                                  |

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| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 32068            | 32068                          | 0.00                                    | 26.81                                      |
| 35074            | 35074                          | 0.00                                    | 16.42                                      |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Anise oil, organic**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30670-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 448 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 | 26735-111137      | 2       |
| Taoasis                | Anise oil, organic | 26735-108555      | 1       |
| Taoasis                | Anise oil, organic | 26735-110455      | 1       |
| 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 | 42803-290         | 1       |
| Taoasis                | Anise oil, organic | 42803-127333      | 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 | 26735-111137      | 2       |
| Taoasis/Sanacorp       | Anise oil, organic | 26735-112250      | 1       |
| Apotheker S Bauer&Comp | Anise oil, organic |                   | 1       |
| Taoasis                | Anise oil, organic | 1492-125379       | 2       |

- 9262 spectra from 770 *Apo-Ident* customers from a total of 3647 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              | 24 565        |
| Type B | 0              | 134           | 26             | 20 761        |
| Type C | 0              | 29            | 4              | 9262          |

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 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| Type B | 100.0000 % (> 99.9458 %) | 83.7500 % (> 81.8750 %)  |
| Type C | 100.0000 % (> 98.7999 %) | 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 | 44.59                  | —                              |
| Basil oil  | 83.67                  | —                              |

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                         | 44.59                           |
| 32794     | 32794               | 0.00                         | 46.55                           |
| 32935     | 32935               | 0.00                         | 49.72                           |

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





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Argan oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 32168-2021-06-11  
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/substance group | 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 54 961 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.
- 24 605 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 18122701 | 1       |
| Caesar & Loretz GmbH | Argan oil | 19116406 | 1       |

- 9292 spectra from 772 *Apo-Ident* customers from a total of 3672 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 24 605        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 3             | 0              | 9292          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8196 %) | 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               | 10.67                  | –                              |
| Excipial® almond oil ointment | 24.78                  | –                              |
| Wax ointment (stabilised)     | 59.86                  | –                              |

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                         | 17.79                           |
| 32571     | 32571               | 0.00                         | 14.37                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Balm Bio Nature**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31645-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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      |

- 9283 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 12            | 0              | 9283          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8033 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------------------------------|---------------------------|-----------------------------------|
| Excipial <sup>®</sup> almond oil ointment | 10.74                     | –                                 |
| Argan oil                                 | 14.03                     | –                                 |
| Wax ointment (stabilised)                 | 43.53                     | –                                 |
| Salicylic white paraffin 10%              | 52.48                     | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31645     | 31645                  | 0.00                            | 15.94                              |
| 31724     | 31724                  | 0.00                            | 19.83                              |
| 32994     | 32994                  | 0.00                            | 10.74                              |
| 34115     | 34115                  | 0.00                            | 19.59                              |

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 2.4-2021-02

Validated substance/substance group **Banana aroma**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31105-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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.

- 21 spectra from 17 *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 | 14353709  | 1       |
| Caelo                      | Banana aroma | 16089304  | 2       |
| Caelo                      | Banana aroma | 17189001  | 4       |
| Caelo                      | Banana aroma | 17189002  | 2       |
| 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       | Banana aroma | 191853001 | 1       |
| Caesar & Loretz GmbH/Sa... | Banana aroma | 19185301  | 1       |
| Caelo                      | Banana aroma | 12302509  | 1       |

- 9274 spectra from 772 *Apo-Ident* customers from a total of 3663 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              | 24 565        |
| Type B | 0              | 80            | 0              | 20 881        |
| Type C | 0              | 21            | 0              | 9274          |

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 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| Type B | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| Type C | 100.0000 % (> 98.8010 %) | 100.0000 % (> 71.4286 %) |

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *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  | 115.63                 | —                              |

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                         | 173.28                          |
| 31606     | 31606               | 0.00                         | 172.49                          |
| 33687     | 33687               | 0.00                         | 171.17                          |

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 2.4-2021-02

Validated substance/substance group **Basil oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30751-2021-06-11  
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/substance group | 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 54 961 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.
- 24 605 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 841 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 24 605        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------------|---------------------------|-----------------------------------|
| Anise oil, organic | 89.27                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31755     | 31755                  | 0.00                            | 153.33                             |
| 33725     | 33725                  | 0.00                            | 159.78                             |

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 2.4-2021-02

Validated substance/substance group **Benzoin siam oil 20%**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30456-2021-06-11  
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/substance group | 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 54 961 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.
- 24 485 spectra from a total of 504 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 449 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% | 548481-111780 | 1       |
| Taoasis  | Benzoin siam oil 20% | 541389-111081 | 1       |
| Taoasis  | Benzoin siam oil 20% | 23478-116955  | 2       |
| Taoasis  | Benzoin siam oil 20% | 17578-116819  | 1       |
| Taoasis  | Benzoin siam oil 20% | 548442-113119 | 1       |
| Taoasis  | Benzoin siam oil 20% | 31343-118365  | 1       |
| Taoasis  | Benzoin siam oil 20% | 41242-121512  | 1       |
| Taoasis  | Benzoin siam oil 20% | 54125         | 1       |
| Taoasis  | Benzoin siam oil 20% | 41242-120661  | 1       |
| Taoasis  | Benzoin siam oil 20% | 59023-125420  | 1       |
| Taoasis  | Benzoin siam oil 20% | 62330-124547  | 1       |
| Taoasis  | Benzoin siam oil 20% | 474084-96350  | 1       |
| Taoasis  | Benzoin siam oil 20% | 51939-123084  | 1       |
| Taoasis  | Benzoin siam oil 20% | 63287-126233  | 1       |

- 9279 spectra from 772 *Apo-Ident* customers from a total of 3660 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              | 24 485        |
| Type B | 0              | 67            | 13             | 20 881        |
| Type C | 0              | 15            | 1              | 9279          |

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 % (> 99.9603 %) | 100.0000 % (> 97.2727 %) |
| Type B | 100.0000 % (> 99.9456 %) | 83.7500 % (> 80.0000 %)  |
| Type C | 100.0000 % (> 98.8020 %) | 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 | 90.91                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31256     | 31256               | 0.00                         | 91.22                           |
| 31843     | 31843               | 0.00                         | 90.91                           |
| 32974     | 32974               | 0.00                         | 96.04                           |
| 33855     | 33855               | 0.00                         | 98.11                           |
| 33944     | 33944               | 0.00                         | 100.49                          |

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

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





# VALIDATION REPORT

## IdentModule 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Bepanthen® Wund- und Heilsalbe</b>                           |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 31048-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group      | Type A | Type B | Type C |
|--------------------------------|--------|--------|--------|
| Bepanthen® Wund- und Heilsalbe | 3      | 2      | 3      |

## Second-stage model

For differentiation of the substance/substance group *Bepanthen<sup>®</sup> 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<sup>®</sup> Wund- und Heilsalbe*:

| Supplier | Substance                       | Batch   | Sample ID | Spectra | Certificate  |
|----------|---------------------------------|---------|-----------|---------|--------------|
| Bayer    | Bepanthen <sup>®</sup> Wund-... | GP00LB9 | 31048     | 40      | not required |
| Bayer    | Bepanthen <sup>®</sup> Wund-... | GP012SS | 31758     | 60      | not required |
| Bayer    | Bepanthen <sup>®</sup> Wund-... | GP01CTH | 33613     | 40      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> Wund- und Heilsalbe*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> Wund- und Heilsalbe | GP018T5 | 32720     | 40      |
| Bayer    | Bepanthen <sup>®</sup> Wund- und Heilsalbe | GP019ZF | 32948     | 40      |

- 20 881 spectra from a total of 449 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 3 *Apo-Ident* customers from 3 batches from the substance/substance group *Bepanthen® Wund- und Heilsalbe*.
- 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 |
|-----------|--------------------------------|----------|---------|
| Bayer     | Bepanthen® Wund- und Heilsalbe | GP01R60  | 1       |
| Bayer     | Bepanthen® Wund- und Heilsalbe | GP01AUE  | 1       |
| Bombastus | Bepanthen® Wund- und Heilsalbe | GP01-DR9 | 1       |

- 9292 spectra from 772 *Apo-Ident* customers from a total of 3672 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 3             | 0              | 9292          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8196 %) | 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*<sup>®</sup> *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<br>main model | Distance in<br>second-stage model |
|-----------------------------------|---------------------------|-----------------------------------|
| Asche Basis <sup>®</sup> ointment | 14.20                     | —                                 |
| Neribas <sup>®</sup> ointment     | 19.64                     | —                                 |
| Alfason Basis Cresa <sup>®</sup>  | 35.29                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Bepanthen*<sup>®</sup> *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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31048     | 31048                  | 0.00                            | 31.12                              |
| 31758     | 31758                  | 0.00                            | 34.43                              |
| 33613     | 33613                  | 0.00                            | 34.55                              |

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 2.4-2021-02

Validated substance/substance group **Bergamot oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30307-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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 | 73340-506            | 1       |
| Taoasis   | Bergamot oil | 77879-3984           | 1       |
| Taoasis   | Bergamot oil | d01be14m-121110bag90 | 1       |

- 9276 spectra from 771 *Apo-Ident* customers from a total of 3657 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 15            | 4              | 9276          |



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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8013 %) | 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.

| <b>Substance</b>          | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|---------------------------|-------------------------------|---------------------------------------|
| Chamomile (essential oil) | 24.49                         | –                                     |
| Spearmint oil             | 36.27                         | –                                     |
| Dwarf pine oil            | 55.51                         | –                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31641            | 31641                      | 0.00                                | 31.72                                  |
| 31760            | 31760                      | 0.00                                | 30.01                                  |
| 31784            | 31784                      | 0.00                                | 28.50                                  |

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



variance of the original reference substance, but cannot add new aspects or forms of the substance.



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30966-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil; Cajeput (essentiell 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/substance group                                | Type A | Type B | Type C |
|----------------------------------------------------------|--------|--------|--------|
| Cajeput oil / Eucalyptus oil / Niaouli oil / Rosmary oil | 17     | 7      | 103    |

## Second-stage model

For differentiation of the substance/substance group *Cajeput oil* / *Eucalyptus oil* / *Niaouli oil* / *Rosemary 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* / *Rosemary 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 54 961 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* / *Rosemary oil*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 17 different batches.
- 23 925 spectra from a total of 492 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 <sup>†</sup>. The following applies to the remaining unmarked samples:

In the same batch, there 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      |

- 20 561 spectra from a total of 442 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) | 131010-115487     | 2       |
| Taoasis   | Cajeput (essentiel oil) | 131010-117241     | 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) | 1518-122790       | 1       |
| Taoasis   | Cajeput (essentiel oil) | 1518-122691       | 1       |
| Taoasis   | Cajeput (essentiel oil) | 1662-124870       | 1       |
| Taoasis   | Cajeput (essentiel oil) | 1724-125910       | 1       |

*continued on the next page*

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| <b>Supplier</b>            | <b>Substance</b>        | <b>Batch</b>      | <b>Spectra</b> |
|----------------------------|-------------------------|-------------------|----------------|
| Taoasis                    | Cajeput (essentiel oil) | 1724-126425       | 1              |
| Taoasis                    | Cajeput (essentiel oil) | 1724-127010       | 2              |
| 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          | 16351312          | 3              |
| Caelo                      | Eucalyptus oil          | 17337701          | 1              |
| Caelo                      | Eucalyptus oil          | 19016712          | 1              |
| Caelo                      | Eucalyptus oil          | 15400202          | 3              |
| Caelo                      | Eucalyptus oil          | 18171714          | 1              |
| 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              |
| Taoasis                    | Eucalyptus oil          | 130205-111868     | 1              |
| Taoasis                    | Eucalyptus oil          | 33364-110871      | 1              |
| Taoasis                    | Eucalyptus oil          | 543495-112704     | 1              |
| Taoasis                    | Eucalyptus oil          | 43703-122178      | 1              |
| Taoasis                    | Eucalyptus oil          | 43703-122404      | 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              |
| Taoasis                    | Eucalyptus oil          | 98937-5299        | 2              |
| Taoasis                    | Eucalyptus oil          | 107371-6271       | 1              |

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| Supplier        | Substance               | Batch          | Spectra |
|-----------------|-------------------------|----------------|---------|
| Bauer           | Niaouli oil             | 6558611608     | 1       |
| Caelo           | Niaouli oil             | 16312603       | 1       |
| Taoasis         | Niaouli oil             | 22553-120413   | 1       |
| Taoasis         | Niaouli oil             | 22553-121510   | 1       |
| Taoasis         | Niaouli oil             | 40428-123092   | 1       |
| Taoasis         | Niaouli oil             | 22553-120482   | 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            | 26057-119164   | 1       |
| Taoasis         | Rosemary oil            | 1526-123355    | 1       |
| Taoasis         | Rosemary oil            | 1526-125088    | 1       |
| Taoasis         | Rosemary oil            | 1614-125089    | 12      |
| Taoasis         | Rosemary oil            | 26057-122996   | 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       |

- 9149 spectra from 771 *Apo-Ident* customers from a total of 3570 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 780           | 0              | 23 925        |
| <b>Type B</b> | 0              | 400           | 0              | 20 561        |
| <b>Type C</b> | 0              | 144           | 2              | 9149          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.2308 %) |
| <b>Type B</b> | 100.0000 % (> 99.9453 %) | 100.0000 % (> 98.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7983 %) | 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 | 11.19                  | —                              |
| Citrus oil           | 25.94                  | —                              |
| Hyssop oil           | 28.84                  | —                              |
| Ravensara oil        | 28.94                  | —                              |
| Myrtle oil           | 31.54                  | —                              |
| Marjoram oil         | 39.71                  | —                              |
| Vetiver bourbon oil  | 41.75                  | —                              |
| Angelica root oil    | 46.18                  | —                              |
| Sage oil             | 46.47                  | —                              |
| Cedar wood oil       | 57.52                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30966     | 30966               | 0.00                         | 38.15                           |
| 31136     | 31136               | 0.00                         | 57.18                           |
| 31420     | 31420               | 0.00                         | 28.84                           |
| 31548     | 31548               | 0.00                         | 50.48                           |
| 31551     | 31551               | 0.00                         | 22.25                           |
| 31691     | 31691               | 0.00                         | 17.07                           |

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| Sample ID | Reference sample ID | Distance to reference sample | Distance to next foreign sample |
|-----------|---------------------|------------------------------|---------------------------------|
| 31694     | 31694               | 0.00                         | 36.42                           |
| 32173     | 32173               | 0.00                         | 56.25                           |
| 32174     | 32174               | 0.00                         | 39.86                           |
| 32903     | 32903               | 0.00                         | 30.72                           |
| 32933     | 32933               | 0.00                         | 30.26                           |
| 32970     | 32970               | 0.00                         | 45.70                           |
| 33657     | 33657               | 0.00                         | 58.94                           |
| 34104     | 34104               | 0.00                         | 24.37                           |
| 34374     | 34374               | 0.00                         | 33.93                           |
| 34380     | 34380               | 0.00                         | 45.38                           |
| 34401     | 34401               | 0.00                         | 62.12                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Camphor oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33826-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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 *Manhattan distance* is specified within the main model and, where appropriate, within the second-stage model.

| Substance         | Distance in<br>main model | Distance in<br>second-stage model |
|-------------------|---------------------------|-----------------------------------|
| Angelica root oil | 22.85                     | —                                 |
| Marjoram oil      | 25.16                     | —                                 |
| Hyssop oil        | 32.62                     | —                                 |
| Citus oil         | 38.27                     | —                                 |
| Cumin oil         | 40.70                     | —                                 |
| Swiss pine oil    | 41.42                     | —                                 |
| Silver fir oil    | 42.59                     | —                                 |
| Cypress oil       | 43.56                     | —                                 |
| Spruce needle oil | 48.54                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33826     | 33826                  | 0.00                            | 31.32                              |
| 33827     | 33827                  | 0.00                            | 30.85                              |

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 2.4-2021-02

Validated substance/substance group **Cardamom oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33813-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------------------|---------------------------|-----------------------------------|
| Citrus oil            | 29.56                     | —                                 |
| Vetiver bourbon oil   | 40.40                     | —                                 |
| Manuka oil            | 43.60                     | —                                 |
| Matricaria oil, roman | 45.03                     | —                                 |
| Sage oil              | 46.20                     | —                                 |
| 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33813     | 33813                  | 0.00                            | 46.26                              |
| 33961     | 33961                  | 0.00                            | 46.20                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Carrot seed oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31555-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 821 spectra from a total of 448 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 140           | 0              | 20 821        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 95.7143 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|------------------|---------------------------|-----------------------------------|
| Marjoram oil     | 22.01                     | —                                 |
| Tea tree oil     | 27.13                     | —                                 |
| Patchouli oil    | 40.02                     | —                                 |
| Thyme oil, white | 46.95                     | —                                 |
| Lemon grass oil  | 53.90                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31555     | 31555                  | 0.00                            | 35.13                              |
| 32812     | 32812                  | 0.00                            | 64.08                              |
| 34282     | 34282                  | 0.00                            | 58.90                              |

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 2.4-2021-02

Validated substance/substance group **Cedar wood oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30654-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 841 spectra from a total of 448 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 | 32812-113008   | 3       |
| Taoasis          | Cedar wood oil | 381008-116967  | 1       |
| Taoasis          | Cedar wood oil | 7711023-120348 | 1       |
| Taoasis          | Cedar wood oil | 7891018-120108 | 1       |
| Taoasis          | Cedar wood oil | 831018-122540  | 1       |
| Taoasis          | Cedar wood oil | 7891019-121034 | 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 | 1627-127827    | 1       |
| Taoasis          | Cedar wood oil | 1802-128288    | 3       |
| Taoasis          | Cedar wood oil | 1802-750       | 3       |
| Taoasis          | Cedar wood oil | 18302-128288   | 1       |
| Taoasis          | Cedar wood oil | 1802-972       | 1       |
| Taoasis          | Cedar wood oil | 1802-1975      | 1       |
| Taoasis          | Cedar wood oil | 2339-3615      | 2       |
| Taoasis          | Cedar wood oil | 2339-3450      | 1       |
| 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       |

- 9264 spectra from 772 *Apo-Ident* customers from a total of 3654 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              | 24 545        |
| Type B | 0              | 80            | 40             | 20 841        |
| Type C | 0              | 31            | 0              | 9264          |

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 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| Type B | 100.0000 % (> 99.9455 %) | 66.6667 % (> 64.1667 %)  |
| Type C | 100.0000 % (> 98.8000 %) | 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 |
|----------------------|------------------------|--------------------------------|
| Citrus oil           | 15.76                  | —                              |
| Hyssop oil           | 20.05                  | —                              |
| Vetiver bourbon oil  | 21.90                  | —                              |
| Ginger oil           | 24.18                  | —                              |
| Marjoram oil         | 25.16                  | —                              |
| Myrtle oil           | 34.61                  | —                              |
| Yarrow oil           | 36.44                  | —                              |
| Salmon oil           | 41.48                  | —                              |
| Angelica root oil    | 43.05                  | —                              |
| Immortelle oil       | 43.66                  | —                              |
| Cypress oil          | 45.90                  | —                              |
| Niaouli oil          | 49.44                  | —                              |
| Carrot seed oil      | 49.70                  | —                              |
| Rosemary camphor oil | 50.15                  | —                              |

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                         | 66.60                           |
| 31851     | 31851               | 0.00                         | 20.05                           |
| 33199     | 33199               | 0.00                         | 64.35                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Chamomile (essential oil)**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33811-2021-06-11  
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/substance group | 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 54 961 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.
- 24 555 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 10      |

- 20 871 spectra from a total of 448 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 150           | 0              | 24 555        |
| <b>Type B</b> | 0              | 67            | 23             | 20 871        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 96.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 74.4444 % (> 71.1111 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | n/a (n/a)                |

<sup>†</sup>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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Bergamot oil    | 19.64                     | —                                 |
| Spearmint oil   | 33.58                     | —                                 |
| Carrot seed oil | 43.26                     | —                                 |
| Lemon grass oil | 49.73                     | —                                 |
| Patchouli oil   | 51.33                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33811     | 33811                  | 0.00                            | 50.31                              |
| 33825     | 33825                  | 0.00                            | 22.49                              |
| 33952     | 33952                  | 0.00                            | 24.63                              |
| 33963     | 33963                  | 0.00                            | 51.08                              |

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 2.4-2021-02

Validated substance/substance group **Cinnamon bark oil, Ceylon**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30957-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 450 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       |

- 9291 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 4             | 0              | 9291          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8142 %) | 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 | 105.03                 | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30957     | 30957               | 0.00                         | 220.76                          |
| 31648     | 31648               | 0.00                         | 174.86                          |
| 34107     | 34107               | 0.00                         | 176.89                          |
| 34375     | 34375               | 0.00                         | 105.03                          |

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 2.4-2021-02

Validated substance/substance group **Citric oil / Lime oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31544-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Citric oil / Lime oil     | 7      | 3      | 51     |

## 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 54 961 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.
- 24 325 spectra from a total of 502 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 701 spectra from a total of 447 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.

- 78 spectra from 62 *Apo-Ident* customers from 52 batches from the substance/substance group *Citric oil / Lime oil*.
- Among them are spectra of independent samples from 51 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier  | Substance  | Batch            | Spectra |
|-----------|------------|------------------|---------|
| Caelo     | Citric oil | 18328003         | 4       |
| 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 | 15182711         | 1       |
| Caelo     | Citric oil | 16275206         | 1       |
| Caelo     | Citric oil | 16028719         | 2       |
| Caelo     | Citric oil | 16275202         | 1       |
| Caelo     | Citric oil | 16275213         | 1       |
| Caelo     | Citric oil | 2416Q-01973      | 1       |
| Caelo     | Citric oil | 16275216         | 4       |
| Caelo     | Citric oil | 17321104         | 2       |
| Caelo     | Citric oil | 16028702         | 3       |
| Caelo     | Citric oil | 18092216         | 2       |
| Caelo     | Citric oil | 91(18092216)     | 1       |
| Caelo     | Citric oil | 14365212         | 3       |
| Caelo     | Citric oil | 15182703         | 3       |
| Caelo     | Citric oil | 14385201         | 1       |
| Caelo     | Citric oil | W373             | 1       |
| Fagron    | Citric oil | 14H06-B02-308273 | 1       |
| Fagron    | Citric oil | 13K14-B03-294704 | 1       |
| Fagron    | Citric oil | 14H06-B02-299949 | 1       |
| Fagron    | Citric oil | 15F29-804        | 1       |

*continued on the next page*



continued from previous page

| Supplier          | Substance  | Batch            | Spectra |
|-------------------|------------|------------------|---------|
| Fagron            | Citric oil | 15f29-b04-325354 | 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 | 15F29-B04        | 2       |
| Fagron            | Citric oil | 19K11-F08        | 1       |
| Caelo             | Citric oil | 17106807         | 5       |
| Fagron            | Citric oil | 15F29-B04-322985 | 1       |
| Kögl              | Citric oil | 182006163916     | 1       |
| Caelo             | Citric oil | 18092202         | 3       |
| Fagron            | Citric oil | 17B14B04341736   | 1       |
| Primavera/ Phönix | Citric oil | 595G26           | 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       |

- 9217 spectra from 767 *Apo-Ident* customers from a total of 3623 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 be clearly distinguished from all other substances using NIR spectroscopy with *Apo-Ident*. For this purpose, all relevant spectra of the various substances were compared with *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 380           | 0              | 24 325        |
| <b>Type B</b> | 0              | 238           | 22             | 20 701        |
| <b>Type C</b> | 0              | 77            | 1              | 9217          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9602 %) | 100.0000 % (> 98.4211 %) |
| <b>Type B</b> | 100.0000 % (> 99.9453 %) | 91.5385 % (> 90.3846 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7987 %) | 98.7179 % (> 94.8718 %)  |

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



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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *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<br>main model | Distance in<br>second-stage model |
|-------------------------|---------------------------|-----------------------------------|
| Mandarin oil, green     | 17.67                     | —                                 |
| Grapefruit oil, organic | 20.04                     | —                                 |
| Orange oil              | 33.07                     | —                                 |
| Silver fir oil          | 38.68                     | —                                 |
| Tea tree oil            | 48.01                     | —                                 |
| Blood orange oil        | 56.47                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31544     | 31544                  | 0.00                            | 38.68                              |
| 31558     | 31558                  | 0.00                            | 17.68                              |
| 31838     | 31838                  | 0.00                            | 17.37                              |
| 33611     | 33611                  | 0.00                            | 17.08                              |
| 33874     | 33874                  | 0.00                            | 41.48                              |
| 33942     | 33942                  | 0.00                            | 40.78                              |
| 34393     | 34393                  | 0.00                            | 30.67                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Citronella oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31550-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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       |

- 9291 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 4             | 0              | 9291          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8142 %) | 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% | 41.40                  | —                              |
| Palmarosa oil, organic                 | 43.27                  | —                              |
| Lemon grass oil                        | 44.01                  | —                              |
| Marjoram oil                           | 47.14                  | —                              |
| Tea tree oil                           | 48.29                  | —                              |

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                         | 38.93                           |
| 33728     | 33728               | 0.00                         | 34.73                           |
| 34409     | 34409               | 0.00                         | 39.32                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

|                                     |                                                                          |
|-------------------------------------|--------------------------------------------------------------------------|
| Validated substance/substance group | Citrus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                             |
| Report date                         | 11/06/2021                                                               |
| Report number                       | 30961-2021-06-11                                                         |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany          |

### Relevant substance names

Citrus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil; Citrus 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 *Citrus 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 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group                                                             | Type A | Type B | Type C |
|---------------------------------------------------------------------------------------|--------|--------|--------|
| Citrus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop oil | 21     | 15     | 65     |

## 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 54 961 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.
- 23 725 spectra from a total of 488 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 *Citrus 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             | Citrus oil     | 00348C26              | 34178     | 40      |
| Taoasis               | Citrus 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      |

- 20241 spectra from a total of 434 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.

- 105 spectra from 47 *Apo-Ident* customers from 66 batches from the substance/substance group *Citrus oil / Lavender oil / Clary sage oil / Myrtle oil / Petitgrain oil / Hyssop 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 |
|----------|----------------|---------------|---------|
| Taoasis  | Citrus oil     | 1510-1171     | 1       |
| Taoasis  | Citrus oil     | 2345-2578     | 2       |
| Taoasis  | Clary sage oil | 487962-106655 | 1       |
| Taoasis  | Clary sage oil | 2098-119159   | 1       |

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| Supplier                   | Substance      | Batch               | Spectra |
|----------------------------|----------------|---------------------|---------|
| Taoasis                    | Clary sage oil | 10140-146           | 1       |
| Taoasis                    | Clary sage oil | 1700-125289         | 2       |
| Taoasis                    | Clary sage oil | 13304-5798          | 2       |
| 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   | 277818              | 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   | 2/2015-125808I09    | 12      |
| Taoasis                    | Lavender oil   | 34/151/16           | 1       |
| Taoasis                    | Lavender oil   | 22015-126998        | 3       |
| Taoasis                    | Lavender oil   | 22015-128587        | 1       |
| Taoasis                    | Lavender oil   | 22015-508           | 5       |
| 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   | 96336-5473          | 2       |
| Taoasis                    | Lavender oil   | 160802301/2016-1909 | 1       |
| Taoasis                    | Lavender oil   | 170124022016-5298   | 1       |
| 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       |
| Taoasis/Phoenix/10.02.2... | Lavender oil   | 5083                | 1       |

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

- 9190 spectra from 766 *Apo-Ident* customers from a total of 3609 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 *Citrus 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 *Citrus 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 980           | 0              | 23 725        |
| <b>Type B</b> | 0              | 710           | 10             | 20 237        |
| <b>Type C</b> | 0              | 105           | 0              | 9190          |

The substance/substance group *Citrus 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.3878 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 98.6111 % (> 98.1944 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7985 %) | 100.0000 % (> 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 *Citrus 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 | 20.17                  | —                              |
| Neroli oil    | 28.69                  | —                              |

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| Substanz             | Distance in<br>main model | Distance in<br>second-stage model |
|----------------------|---------------------------|-----------------------------------|
| Melissa oil 30%      | 29.44                     | —                                 |
| Marjoram oil         | 31.47                     | —                                 |
| Cypress oil          | 31.76                     | —                                 |
| Cedar wood oil       | 32.36                     | —                                 |
| Angelica root oil    | 32.51                     | —                                 |
| Rosemary camphor oil | 35.39                     | —                                 |
| Thyme oil, white     | 37.89                     | —                                 |
| Vetiver bourbon oil  | 38.14                     | —                                 |
| Sage oil             | 39.03                     | —                                 |
| Yarrow oil           | 40.16                     | —                                 |
| Ginger oil           | 43.59                     | —                                 |
| Niaouli oil          | 45.70                     | —                                 |
| Coriander oil        | 47.09                     | —                                 |
| Rosemary oil         | 50.76                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Citrus 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30961     | 30961                  | 0.00                            | 51.87                              |
| 30962     | 30962                  | 0.00                            | 66.14                              |
| 31649     | 31649                  | 0.00                            | 40.76                              |
| 31669     | 31669                  | 0.00                            | 52.95                              |
| 31756     | 31756                  | 0.00                            | 72.68                              |
| 31778     | 31778                  | 0.00                            | 74.68                              |
| 31782     | 31782                  | 0.00                            | 42.17                              |
| 31850     | 31850                  | 0.00                            | 42.48                              |
| 31852     | 31852                  | 0.00                            | 32.57                              |
| 32980     | 32980                  | 0.00                            | 20.17                              |
| 33024     | 33024                  | 0.00                            | 64.53                              |
| 33033     | 33033                  | 0.00                            | 54.38                              |
| 33760     | 33760                  | 0.00                            | 40.03                              |
| 33797     | 33797                  | 0.00                            | 34.54                              |
| 33804     | 33804                  | 0.00                            | 71.80                              |
| 33816     | 33816                  | 0.00                            | 32.36                              |
| 33830     | 33830                  | 0.00                            | 44.09                              |
| 33957     | 33957                  | 0.00                            | 35.94                              |
| 34294     | 34294                  | 0.00                            | 33.57                              |
| 34367     | 34367                  | 0.00                            | 80.79                              |
| 34395     | 34395                  | 0.00                            | 34.60                              |

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 2.4-2021-02

Validated substance/substance group **Clove oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31270-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 450 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       |

- 9284 spectra from 771 *Apo-Ident* customers from a total of 3665 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 10            | 1              | 9284          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8038 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Siam benzoin | 420.26                    | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31035     | 31035                  | 0.00                            | 437.42                             |
| 31270     | 31270                  | 0.00                            | 437.29                             |
| 31557     | 31557                  | 0.00                            | 420.26                             |
| 31683     | 31683                  | 0.00                            | 427.05                             |

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 2.4-2021-02

Validated substance/substance group **Common wormwood oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30842-2021-06-11  
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/substance group | 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 54 961 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.
- 24 605 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 761 spectra from a total of 449 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 24 605        |
| <b>Type B</b> | 0              | 53            | 147            | 20 761        |
| <b>Type C</b> | 0              | 0             | 1              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 26.5000 % (> 25.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Thuja oil | 55.31                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31637     | 31637                  | 0.00                            | 68.52                              |
| 34209     | 34209                  | 0.00                            | 82.53                              |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Contramarum aroma</b>                                        |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 31007-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Contramarum aroma         | 3      | 3      | 66     |

## 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 54 961 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.
- 24 585 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 841 spectra from a total of 448 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.

- 166 spectra from 70 *Apo-Ident* customers from 67 batches from the substance/substance group *Contramarum aroma*.
- Among them are spectra of independent samples from 66 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 | 7071207      | 1       |
| Caelo               | Contramarum aroma | 12201407     | 2       |
| 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 | 16083805     | 1       |
| Caelo               | Contramarum aroma | 16083806     | 1       |
| Caelo               | Contramarum aroma | 16267102     | 4       |
| Caelo               | Contramarum aroma | 17223002     | 4       |
| Caelo               | Contramarum aroma | 19121701     | 1       |
| Caelo               | Contramarum aroma | 17223007     | 6       |
| 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 | 17223005     | 4       |
| Caelo               | Contramarum aroma | 13411011     | 1       |
| Caelo               | Contramarum aroma | 19209402     | 1       |
| Caelo               | Contramarum aroma | 7082006      | 1       |
| Caelo               | Contramarum aroma | 14320015     | 3       |
| Caelo               | Contramarum aroma | 16083801     | 8       |
| 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 | 19209403     | 2       |
| Caelo               | Contramarum aroma | 21(17223001) | 1       |
| Caelo               | Contramarum aroma | 16267101     | 5       |
| Caelo               | Contramarum aroma | 14320001     | 1       |
| Caelo               | Contramarum aroma | 16083804     | 2       |
| Caelo               | Contramarum aroma | 16267103     | 4       |

*continued on the next page*

continued from previous page

| Supplier                   | Substance         | Batch       | Spectra |
|----------------------------|-------------------|-------------|---------|
| Caelo                      | Contramarum aroma | 17223001    | 7       |
| Caelo                      | Contramarum aroma | 14320009    | 2       |
| Caelo                      | Contramarum aroma | 15113003    | 2       |
| Caelo                      | Contramarum aroma | 143200009   | 1       |
| Caelo                      | Contramarum aroma | 16083802    | 2       |
| Caelo                      | Contramarum aroma | 19129002    | 1       |
| Caelo                      | Contramarum aroma | 169267103   | 1       |
| Caelo                      | Contramarum aroma | 17223008    | 2       |
| Caelo                      | Contramarum aroma | 18106702    | 6       |
| Caelo                      | Contramarum aroma | 18106703    | 9       |
| Caelo                      | Contramarum aroma | 19065401    | 11      |
| 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    | 5       |
| Caesar & Loretz GmbH       | Contramarum aroma | 19129001    | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 19209402    | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 19129002    | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 192867003   | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 19209403    | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 192867006   | 1       |
| Caesar & Loretz GmbH       | Contramarum aroma | 20000961005 | 1       |
| Caesar & Loretz GmbH/No... | Contramarum aroma | 19065401    | 1       |
| Caesar & Loretz GmbH/No... | Contramarum aroma | 20000961004 | 1       |
| Caesar & Loretz GmbH/Ph... | Contramarum aroma | 192867004   | 1       |
| Fagron                     | Contramarum aroma | 16083801    | 1       |
| Fiebig                     | Contramarum aroma | 11378810    | 1       |
| Gehe                       | Contramarum aroma | 12201404    | 1       |
| 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       |

- 9129 spectra from 764 *Apo-Ident* customers from a total of 3608 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              | 24 585        |
| Type B | 0              | 117           | 3              | 20 841        |
| Type C | 0              | 148           | 18             | 9129          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 97.5000 % (> 95.0000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7983 %) | 89.1566 % (> 87.3494 %)  |

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

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

Where the number of spectra does 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.

| <b>Substance</b> | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|------------------|-------------------------------|---------------------------------------|
| Raspberry aroma  | 41.99                         | —                                     |
| Strawberry aroma | 109.69                        | —                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31007            | 31007                      | 0.00                                | 59.73                                  |
| 31289            | 31289                      | 0.00                                | 55.73                                  |
| 31398            | 31398                      | 0.00                                | 58.42                                  |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Cumin oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30449-2021-06-11  
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/substance group | 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 54 961 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.
- 24 585 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 121217-111221       | 1       |
| Taoasis        | Cumin oil | 24081-106027        | 1       |
| Taoasis        | Cumin oil | 104723-298          | 1       |
| Taoasis/Noweda | Cumin oil | 51764-124373BAG9045 | 1       |

- 9291 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 24 585        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 3             | 1              | 9291          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8142 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------|---------------------------|-----------------------------------|
| Marjoram oil | 132.11                    | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31141     | 31141                  | 0.00                            | 141.37                             |
| 32267     | 32267                  | 0.00                            | 139.43                             |
| 32904     | 32904                  | 0.00                            | 144.63                             |

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 2.4-2021-02

Validated substance/substance group **Cypress oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30457-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 448 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 | 33720-115882  | 1       |
| Taoasis  | Cypress oil | 487749-107790 | 1       |
| Taoasis  | Cypress oil | 514085-111139 | 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 | 107527-125443 | 2       |
| Taoasis  | Cypress oil | 107527-125965 | 1       |
| Taoasis  | Cypress oil | 341012-123298 | 1       |
| Taoasis  | Cypress oil | 107527-27014  | 1       |
| Taoasis  | Cypress oil | 107527-127323 | 6       |
| Taoasis  | Cypress oil | 45953-129229  | 1       |
| Taoasis  | Cypress oil | 43953-129229  | 1       |

- 9271 spectra from 772 *Apo-Ident* customers from a total of 3660 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              | 24 525        |
| Type B | 0              | 148           | 12             | 20 801        |
| Type C | 0              | 23            | 1              | 9271          |

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 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| Type B | 100.0000 % (> 99.9454 %) | 92.5000 % (> 90.6250 %)  |
| Type C | 100.0000 % (> 98.8006 %) | 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 |
|--------------|------------------------|--------------------------------|
| Citrus oil   | 30.13                  | —                              |
| Marjoram oil | 30.33                  | —                              |
| Myrtle oil   | 34.25                  | —                              |
| Ginger oil   | 48.07                  | —                              |
| Tea tree oil | 51.10                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31656     | 31656               | 0.00                         | 70.78                           |
| 33623     | 33623               | 0.00                         | 68.51                           |
| 33802     | 33802               | 0.00                         | 49.06                           |
| 33954     | 33954               | 0.00                         | 49.57                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Dermatop<sup>®</sup> base ointment**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31060-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Dermatop<sup>®</sup> base ointment

### Special notes

When selecting the *Dermatop<sup>®</sup> 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/substance group           | Type A | Type B | Type C |
|-------------------------------------|--------|--------|--------|
| Dermatop <sup>®</sup> base ointment | 2      | 2      | 34     |

## Second-stage model

For differentiation of the substance/substance group *Dermatop<sup>®</sup> 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<sup>®</sup> base ointment*:

| Supplier       | Substance                       | Batch  | Sample ID | Spectra | Certificate  |
|----------------|---------------------------------|--------|-----------|---------|--------------|
| Sanofi aventis | Dermatop <sup>®</sup> base o... | 3F052A | 31060     | 40      | not required |
| Sanofi aventis | Dermatop <sup>®</sup> base o... | 5F080A | 31717     | 60      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> base ointment*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 24 605 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> base ointment | 5F089A | 32718     | 40      |
| Sanofi aventis | Dermatop <sup>®</sup> base ointment | 7F106A | 33965     | 40      |



- 20 881 spectra from a total of 449 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 20 *Apo-Ident* customers from 35 batches from the substance/substance group *Dermatop<sup>®</sup> base 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                      | Dermatop <sup>®</sup> base ointment | 5F080A | 1       |
| Caelo                      | Dermatop <sup>®</sup> base ointment | 8F124A | 1       |
| Caelo                      | Dermatop <sup>®</sup> base ointment | 7F107A | 1       |
| Phönix                     | Dermatop <sup>®</sup> base ointment | 7F108B | 1       |
| Phönix/ Sanofi/ 02.10.2... | Dermatop <sup>®</sup> base ointment | F136A  | 1       |
| Sanacorp/ Sanofi           | Dermatop <sup>®</sup> base ointment | 9F128A | 1       |
| Sanacorp/Sanofi WE:22.0... | Dermatop <sup>®</sup> base ointment | 5F086A | 1       |
| Sanofi                     | Dermatop <sup>®</sup> base ointment | 8F116A | 1       |
| Sanofi                     | Dermatop <sup>®</sup> base ointment | 9F178A | 1       |
| Sanofi                     | Dermatop <sup>®</sup> base ointment | 9F129A | 2       |
| Sanofi - Noweda            | Dermatop <sup>®</sup> base ointment | 5F089A | 1       |
| Sanofi / Alliance Healt... | Dermatop <sup>®</sup> base ointment | 6F094A | 1       |
| Sanofi / Gehe              | Dermatop <sup>®</sup> base ointment | 6F099A | 1       |
| Sanofi / Sanacorp          | Dermatop <sup>®</sup> base ointment | 8F125A | 1       |
| Sanofi /Noweda             | Dermatop <sup>®</sup> base ointment | 8F121A | 1       |
| Sanofi /Noweda             | Dermatop <sup>®</sup> base ointment | 0F135A | 1       |
| Sanofi /Noweda             | Dermatop <sup>®</sup> base ointment | 0F137A | 1       |
| Sanofi/ Noweda/ 09.04.2... | Dermatop <sup>®</sup> base ointment | F140A  | 1       |
| Sanofi/Alliance            | Dermatop <sup>®</sup> base ointment | 8F119A | 1       |
| Sanofi/Gehe                | Dermatop <sup>®</sup> base ointment | 5F078A | 1       |
| Sanofi/GEHE                | Dermatop <sup>®</sup> base ointment | 8F117A | 1       |
| Sanofi/GEHE                | Dermatop <sup>®</sup> base ointment | 8F115A | 1       |
| Sanofi/GEHE                | Dermatop <sup>®</sup> base ointment | 8F116A | 1       |
| Sanofi/GEHE                | Dermatop <sup>®</sup> base ointment | 8F126A | 1       |
| Sanofi/Kehr                | Dermatop <sup>®</sup> base ointment | 6F099A | 1       |
| Sanofi/Kehr                | Dermatop <sup>®</sup> base ointment | 6F094A | 1       |
| Sanofi/Phoenix             | Dermatop <sup>®</sup> base ointment | 8F120A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 7F109A | 2       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 7F105A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F113A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F114A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F116A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F119A | 2       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F118B | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F121A | 3       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F1238 | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F125A | 2       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 8F126A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 9F127A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 9F131A | 1       |
| Sanofi/Phönix              | Dermatop <sup>®</sup> base ointment | 9F134A | 1       |

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| Supplier       | Substance                           | Batch  | Spectra |
|----------------|-------------------------------------|--------|---------|
| Sanofi/Phönix  | Dermatop <sup>®</sup> base ointment | F137A  | 1       |
| Sanofi/Phönix  | Dermatop <sup>®</sup> base ointment | F140A  | 1       |
| Sanofi-Aventis | Dermatop <sup>®</sup> base ointment | 7F103A | 1       |

- 9245 spectra from 772 *Apo-Ident* customers from a total of 3640 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<sup>®</sup> 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<sup>®</sup> 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 24 605        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 48            | 2              | 9245          |

The substance/substance group *Dermatop<sup>®</sup> 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7992 %) | 96.0000 % (> 90.0000 %)  |

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

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

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

## Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Dermatop<sup>®</sup> 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 <sup>®</sup> H fat N      | 19.63                  | —                              |
| Excipial <sup>®</sup> lipo cream | 20.22                  | —                              |
| Linola <sup>®</sup> fat cream    | 23.51                  | —                              |
| Alfason Basis Cresa <sup>®</sup> | 27.98                  | —                              |
| Alfason <sup>®</sup> Repair      | 36.60                  | —                              |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dermatop<sup>®</sup> 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31060     | 31060               | 0.00                         | 21.22                           |
| 31717     | 31717               | 0.00                         | 24.97                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Dexeryl®**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31512-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Dexeryl®                  | 3      | 2      | 16     |

## Second-stage model

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

*no second-stage model*

## Calibration samples

Only spectra which have been recorded by *HiperScan 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*<sup>®</sup>:

| Supplier     | Substance            | Batch  | Sample ID | Spectra | Certificate  |
|--------------|----------------------|--------|-----------|---------|--------------|
| Pierre Fabre | Dexeryl <sup>®</sup> | G99016 | 31512     | 60      | not required |
| Pierre Fabre | Dexeryl <sup>®</sup> | G00419 | 31630     | 60      | not required |
| Pierre Fabre | Dexeryl <sup>®</sup> | G00650 | 33635     | 40      | not required |

## Validation samples

A total of 54 961 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*<sup>®</sup>. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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*<sup>®</sup>.
- 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 <sup>®</sup> | G00623 | 32762     | 40      |
| Pierre Fabre | Dexeryl <sup>®</sup> | G00658 | 33945     | 40      |

- 20 881 spectra from a total of 449 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       |
| PierreFabre/Now        | Dexeryl®  | G00577        | 1       |
| Pierre Fabre / phoenix | Dexeryl®  | 600869        | 1       |
| Pierre Fabre /Noweda   | Dexeryl®  | G00606        | 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       |

- 9275 spectra from 771 *Apo-Ident* customers from a total of 3659 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 20            | 0              | 9275          |

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

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8011 %) | 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*<sup>®</sup> 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.

| <b>Substance</b>                              | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|-----------------------------------------------|-------------------------------|---------------------------------------|
| Neuroderm <sup>®</sup> moisturising cream     | 16.46                         | —                                     |
| Neuroderm <sup>®</sup> care lotion            | 19.76                         | —                                     |
| Base cream Taoasis                            | 20.41                         | —                                     |
| Excipial <sup>®</sup> U10 Lipolotio           | 22.83                         | —                                     |
| Hans Karrer Lipolotion MicroSilver            | 28.05                         | —                                     |
| Dimeticone ointment 10% SR                    | 29.97                         | —                                     |
| Eucerinum O/W basis                           | 30.42                         | —                                     |
| Abitima <sup>®</sup> clinic body cream        | 32.24                         | —                                     |
| Neribas <sup>®</sup> cream                    | 34.79                         | —                                     |
| DMS <sup>®</sup> base cream high classic      | 34.88                         | —                                     |
| DMS <sup>®</sup> base cream high classic plus | 35.49                         | —                                     |
| Asche Basis <sup>®</sup> lotion               | 36.27                         | —                                     |
| Abitima <sup>®</sup> clinic face cream        | 37.12                         | —                                     |
| La Roche-Posay Toleriane                      | 37.36                         | —                                     |
| Fabitol <sup>®</sup> base cream               | 37.73                         | —                                     |
| DMS <sup>®</sup> base cream classic           | 39.76                         | —                                     |
| Eucerinum W/O basis                           | 44.21                         | —                                     |
| Hans Karrer Lipocream MicroSilver             | 44.24                         | —                                     |
| Optiderm <sup>®</sup> lotion                  | 44.99                         | —                                     |
| Linola <sup>®</sup> body milk                 | 45.50                         | —                                     |
| Asche Basis <sup>®</sup> cream                | 45.87                         | —                                     |
| Excipial <sup>®</sup> U Lipolotio             | 50.50                         | —                                     |

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

### Identity according to identity test using NIR spectroscopy

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



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

| Sample ID | Reference sample ID | Distance to reference sample | Distance to next foreign sample |
|-----------|---------------------|------------------------------|---------------------------------|
| 31512     | 31512               | 0.00                         | 20.38                           |
| 31630     | 31630               | 0.00                         | 27.60                           |
| 33635     | 33635               | 0.00                         | 24.90                           |

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 2.4-2021-02

Validated substance/substance group **Dichloroacetic acid**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30417-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Dichloroacetic acid; Acidum dichloroaceticum

### 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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 10            | 30             | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 25.0000 % (> 17.5000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------|---------------------------|-----------------------------------|
| Nicotine  | 164.07                    | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31642     | 31642                  | 0.00                            | 221.69                             |
| 32750     | 32750                  | 0.00                            | 213.98                             |
| 33794     | 33794                  | 0.00                            | 230.07                             |

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 2.4-2021-02

Validated substance/substance group **Dimeticone ointment 10% SR / Optiderm<sup>®</sup> lotion**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31243-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Dimeticone ointment 10% SR / Optiderm<sup>®</sup> lotion; Dimeticone ointment 10% SR; Optiderm<sup>®</sup> lotion;  
Unguentum dimeticoni 10% SR

### Special notes

When selecting the *Dimeticone ointment 10% SR / Optiderm<sup>®</sup> 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/substance group                                 | Type A | Type B | Type C |
|-----------------------------------------------------------|--------|--------|--------|
| Dimeticone ointment 10% SR / Optiderm <sup>®</sup> lotion | 6      | 2      | 27     |

## Second-stage model

For differentiation of the substance/substance group *Dimeticone ointment 10% SR / Optiderm<sup>®</sup> 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<sup>®</sup> 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 <sup>®</sup> lotion | 341431    | 31266     | 40      | not required |
| Almirall | Optiderm <sup>®</sup> lotion | 511951    | 31759     | 60      | not required |
| Almirall | Optiderm <sup>®</sup> lotion | 706961    | 33268     | 40      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> lotion*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 24 435 spectra from a total of 503 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> lotion | 633771    | 32757     | 20      |
| Almirall | Optiderm <sup>®</sup> lotion | 706961    | 33267     | 40      |

- 20 861 spectra from a total of 448 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<sup>®</sup> 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 | 4A080414  | 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/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       |

- 9260 spectra from 770 *Apo-Ident* customers from a total of 3646 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              | 24 435        |
| Type B | 0              | 100           | 0              | 20 861        |
| Type C | 0              | 35            | 0              | 9260          |

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 % (> 99.9603 %) | 100.0000 % (> 97.7778 %) |
| Type B | 100.0000 % (> 99.9455 %) | 100.0000 % (> 94.0000 %) |
| Type C | 100.0000 % (> 98.7997 %) | 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            | 10.99                  | —                              |
| Hans Karrer Lipolotion MicroSilver | 12.90                  | —                              |
| Asche Basis® lotion                | 18.35                  | —                              |
| Abitima® clinic face cream         | 20.37                  | —                              |
| Eucerinum W/O basis                | 20.58                  | —                              |
| Base cream Taoasis                 | 25.81                  | —                              |
| Dexeryl®                           | 28.29                  | —                              |
| DMS® base cream high classic       | 28.57                  | —                              |
| La Roche-Posay Toleriane           | 28.88                  | —                              |
| Excipial® U10 Lipolotio            | 29.01                  | —                              |
| Excipial® U Lipolotio              | 30.21                  | —                              |

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| Substanz                                      | Distance in<br>main model | Distance in<br>second-stage model |
|-----------------------------------------------|---------------------------|-----------------------------------|
| Neribas <sup>®</sup> cream                    | 31.96                     | —                                 |
| Eucerinum O/W basis                           | 36.07                     | —                                 |
| Neuroderm <sup>®</sup> moisturising cream     | 37.88                     | —                                 |
| Abitima <sup>®</sup> clinic body cream        | 38.85                     | —                                 |
| Asche Basis <sup>®</sup> cream                | 40.68                     | —                                 |
| Fabitol <sup>®</sup> base cream               | 41.39                     | —                                 |
| DMS <sup>®</sup> base cream high classic plus | 45.01                     | —                                 |
| Amciderm <sup>®</sup> Base cream              | 47.37                     | —                                 |
| Hans Karrer Lipocream MicroSilver             | 47.71                     | —                                 |
| Dermatop <sup>®</sup> base cream              | 48.27                     | —                                 |
| Linola <sup>®</sup> body milk                 | 49.38                     | —                                 |
| Allergika <sup>®</sup> Base cream             | 50.54                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Dimeticone ointment 10% SR / Optiderm<sup>®</sup> 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31243     | 31243                  | 0.00                            | 20.59                              |
| 31266     | 31266                  | 0.00                            | 17.33                              |
| 31638     | 31638                  | 0.00                            | 20.44                              |
| 31759     | 31759                  | 0.00                            | 10.99                              |
| 33041     | 33041                  | 0.00                            | 19.13                              |
| 33268     | 33268                  | 0.00                            | 13.58                              |

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 2.4-2021-02

Validated substance/substance group **Dwarf pine oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31542-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 8238-126318 | 1       |
| Taoasis         | Dwarf pine oil | 8783-125163 | 5       |
| Taoasis         | Dwarf pine oil | 8783-127332 | 2       |
| Taoasis/Taoasis | Dwarf pine oil | 25599120877 | 1       |
| Taoasis         | Dwarf pine oil | 11148-1980  | 1       |

- 9283 spectra from 772 *Apo-Ident* customers from a total of 3668 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 104           | 16             | 20 841        |
| <b>Type C</b> | 0              | 9             | 3              | 9283          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 86.6667 % (> 84.1667 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8033 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Spearmint oil       | 20.62                     | —                                 |
| Angelica root oil   | 21.54                     | —                                 |
| Swiss pine oil      | 34.18                     | —                                 |
| Spruce needle oil   | 36.40                     | —                                 |
| Juniper oil         | 38.52                     | —                                 |
| Pine silvestris oil | 43.86                     | —                                 |
| Silver fir oil      | 43.95                     | —                                 |
| Ginger oil          | 45.44                     | —                                 |
| Citrus oil          | 48.52                     | —                                 |
| Citric oil          | 52.51                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31542     | 31542                  | 0.00                            | 29.60                              |
| 31689     | 31689                  | 0.00                            | 30.03                              |
| 32937     | 32937                  | 0.00                            | 21.54                              |
| 34109     | 34109                  | 0.00                            | 29.76                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Ethanol 70% pure / denatured**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30779-2021-06-11  
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/substance group    | Type A | Type B | Type C |
|------------------------------|--------|--------|--------|
| Ethanol 70% pure / denatured | 4      | 3      | 363    |

## 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20841 spectra from a total of 448 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.

- 500 spectra from 152 *Apo-Ident* customers from 371 batches from the substance/substance group *Ethanol 70% pure / denatured*.
- Among them are spectra of independent samples from 360 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. Plueger/ Noweda/ 02...   | Ethanol 70% pure / denatured | 191121      | 2       |
| 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 | 7028041     | 3       |
| Anzag                       | Ethanol 70% pure / denatured | 7027102     | 1       |
| Anzag/ Otto Fischar GmbH... | 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       |

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| Supplier                   | Substance                    | Batch              | Spectra |
|----------------------------|------------------------------|--------------------|---------|
| Apotheke im Forum          | Ethanol 70% pure / denatured | 300517             | 1       |
| Bahnhof-Apothek/Bahnhof. . | Ethanol 70% pure / denatured | 3819A-03043        | 1       |
| Behlen/Phönix              | Ethanol 70% pure / denatured | 1410T1300816       | 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 | ML0G103/20         | 1       |
| Brennerei Gauß             | Ethanol 70% pure / denatured | ML0G604/2020       | 1       |
| Brennerei Gauß             | Ethanol 70% pure / denatured | ML0G505/2020       | 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 | 60919/50La         | 1       |
| Claudia Lange              | Ethanol 70% pure / denatured | 61010/51La         | 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 | W150605            | 1       |
| Defektur                   | Ethanol 70% pure / denatured | 1MH20150818        | 1       |
| Defektur                   | Ethanol 70% pure / denatured | 60209/51Hk         | 1       |
| Defektur                   | Ethanol 70% pure / denatured | 1716M-03043        | 1       |
| Defektur                   | Ethanol 70% pure / denatured | 1LG20170224        | 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 | 1LG20171108        | 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       |

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| Supplier               | Substance                    | Batch       | Spectra |
|------------------------|------------------------------|-------------|---------|
| 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       |
| Doppeleiche Apotheke   | Ethanol 70% pure / denatured | 150504003   | 1       |
| Doppeleiche Apotheke   | Ethanol 70% pure / denatured | 190219005   | 1       |
| Doppeleiche Apotheke   | Ethanol 70% pure / denatured | 200901002   | 1       |
| Doppeleiche Apotheke   | Ethanol 70% pure / denatured | 200806002   | 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 | 1LG20180530 | 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 | SPV7029     | 1       |
| Eigene Herstellung     | Ethanol 70% pure / denatured | SP70140     | 1       |
| eigenherstellung       | Ethanol 70% pure / denatured | 3818Q-02320 | 1       |
| eigenherstellung       | Ethanol 70% pure / denatured | 1819M-02320 | 2       |
| 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 | 42151-02320 | 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       |

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| Supplier                   | Substance                    | Batch            | Spectra |
|----------------------------|------------------------------|------------------|---------|
| 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 | 321Q-02320       | 1       |
| Eigenherstellung           | Ethanol 70% pure / denatured | 1313I-02320      | 1       |
| Eigenherstellung           | Ethanol 70% pure / denatured | 1823             | 1       |
| Eigenherstellung           | Ethanol 70% pure / denatured | 2613I-03043      | 1       |
| 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/ 25.07... | Ethanol 70% pure / denatured | 7028121          | 1       |
| Fischar/ Phoenix/ 29.08... | Ethanol 70% pure / denatured | 7029031          | 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       |

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| Supplier                   | Substance                    | Batch         | Spectra |
|----------------------------|------------------------------|---------------|---------|
| 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 | 170208        | 1       |
| Gehe/Pflüger               | Ethanol 70% pure / denatured | 170308        | 1       |
| Gehe/Pflüger               | Ethanol 70% pure / denatured | 170419        | 2       |
| 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/AllianceH.       | 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 | 1015I-02320   | 1       |
| HirschApotheke             | Ethanol 70% pure / denatured | 2315I-02320   | 1       |
| HirschApotheke             | Ethanol 70% pure / denatured | 4614A-02320   | 1       |
| Hoffmann                   | Ethanol 70% pure / denatured | 781218        | 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       |
| Hofmanns / Noweda          | Ethanol 70% pure / denatured | 820419        | 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       |
| Kehr/Pflüger               | Ethanol 70% pure / denatured | 200302        | 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       |

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| Supplier                   | Substance                    | Batch       | Spectra |
|----------------------------|------------------------------|-------------|---------|
| 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       |
| Kremer GmbH & Co. KG       | Ethanol 70% pure / denatured | 160215      | 1       |
| Kremer GmbH & Co. KG       | Ethanol 70% pure / denatured | 161017      | 1       |
| Kremer GmbH & Co. KG       | Ethanol 70% pure / denatured | 170208      | 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 | 190717      | 4       |

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| <b>Supplier</b>            | <b>Substance</b>             | <b>Batch</b> | <b>Spectra</b> |
|----------------------------|------------------------------|--------------|----------------|
| Noweda                     | Ethanol 70% pure / denatured | 190815       | 2              |
| Noweda                     | Ethanol 70% pure / denatured | 200330       | 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              |
| 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       | 3              |
| Pflüger                    | Ethanol 70% pure / denatured | 190606       | 1              |
| Pflüger                    | Ethanol 70% pure / denatured | 190717       | 1              |
| Pflüger                    | Ethanol 70% pure / denatured | 200310       | 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               | Ethanol 70% pure / denatured | 191121       | 2              |
| Pflüger GmbH & Co.KG       | Ethanol 70% pure / denatured | 170116       | 1              |
| Pflüger GmbH / Gehe        | Ethanol 70% pure / denatured | 180404       | 1              |
| Pflüger GmbH / Noweda      | Ethanol 70% pure / denatured | 190717       | 1              |
| Pflüger GmbH / Noweda      | Ethanol 70% pure / denatured | 200319       | 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/Kehr               | Ethanol 70% pure / denatured | 190430       | 1              |
| Pflüger/Kehr               | Ethanol 70% pure / denatured | 200316       | 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              |

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| Supplier                   | Substance                    | Batch       | Spectra |
|----------------------------|------------------------------|-------------|---------|
| 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-07145 | 1       |
| Rondell Apotheke           | Ethanol 70% pure / denatured | 3414M-02320 | 1       |
| Rondell Apotheke           | Ethanol 70% pure / denatured | 615E-07145  | 1       |
| Rondell Apotheke           | Ethanol 70% pure / denatured | 615E-02320  | 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       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20151222 | 1       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20160304 | 1       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20160721 | 1       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20160921 | 1       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20161011 | 1       |
| selbst hergestellt         | Ethanol 70% pure / denatured | 1MH20170710 | 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       |
| 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       |

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| Supplier      | Substance                    | Batch | Spectra |
|---------------|------------------------------|-------|---------|
| Wolf Apotheke | Ethanol 70% pure / denatured |       | 2       |

- 8795 spectra from 760 *Apo-Ident* customers from a total of 3305 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 484           | 16             | 8795          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7980 %) | 96.8000 % (> 96.2000 %)  |

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

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

Where the number of spectra does 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 | 54.93                  | —                              |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-

stance/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                         | 100.87                          |
| 31055     | 31055               | 0.00                         | 82.88                           |
| 34101     | 34101               | 0.00                         | 95.21                           |
| 34274     | 34274               | 0.00                         | 81.93                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Excipial® almond oil ointment**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30720-2021-06-11  
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/substance group     | Type A | Type B | Type C |
|-------------------------------|--------|--------|--------|
| Excipial® almond oil ointment | 4      | 2      | 36     |

## Second-stage model

For differentiation of the substance/substance group *Excipial<sup>®</sup> 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<sup>®</sup> almond oil ointment*:

| Supplier      | Substance                       | Batch | Sample ID | Spectra | Certificate  |
|---------------|---------------------------------|-------|-----------|---------|--------------|
| Spirig Pharma | Excipial <sup>®</sup> almond... | M023  | 30720     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> almond... | M031  | 31090     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> almond... | N012  | 31278     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> almond... | R012  | 31757     | 60      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> almond oil ointment*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 4 different batches.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> almond oil ointment | S021  | 33209     | 40      |
| Spirig Pharma | Excipial <sup>®</sup> almond oil ointment | T052  | 33210     | 40      |

- 20881 spectra from a total of 449 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.

- 52 spectra from 20 *Apo-Ident* customers from 37 batches from the substance/substance group *Excipial<sup>®</sup> almond oil ointment*.
- Among them are spectra of independent samples from 36 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier                    | Substance                                 | Batch             | Spectra |
|-----------------------------|-------------------------------------------|-------------------|---------|
| Caelo                       | Excipial <sup>®</sup> almond oil ointment | lotno32           | 1       |
| Caelo                       | Excipial <sup>®</sup> almond oil ointment | 20170829Ma2       | 1       |
| Caelo                       | Excipial <sup>®</sup> almond oil ointment | 20170829Ma3       | 1       |
| Ebert & Jacobi              | Excipial <sup>®</sup> almond oil ointment | 50239             | 1       |
| Fiebig                      | Excipial <sup>®</sup> almond oil ointment | S051              | 1       |
| Galderma                    | Excipial <sup>®</sup> almond oil ointment | R043              | 1       |
| Galderma                    | Excipial <sup>®</sup> almond oil ointment | 50498             | 1       |
| Galderma                    | Excipial <sup>®</sup> almond oil ointment | 8774004           | 1       |
| Galderma (Spirig Pharma...) | Excipial <sup>®</sup> almond oil ointment | R043              | 1       |
| Galderma International ...  | Excipial <sup>®</sup> almond oil ointment | T031              | 1       |
| Galderma/Alliance           | Excipial <sup>®</sup> almond oil ointment | V061              | 1       |
| Galderma/Anzag              | Excipial <sup>®</sup> almond oil ointment | S033              | 1       |
| Galderma/Kehr               | Excipial <sup>®</sup> almond oil ointment | T051              | 1       |
| Galderma/Kehr               | Excipial <sup>®</sup> almond oil ointment | V031              | 1       |
| Galderma/Now                | Excipial <sup>®</sup> almond oil ointment | LOTS021           | 1       |
| Galderma/Noweda             | Excipial <sup>®</sup> almond oil ointment | S012              | 1       |
| Galderma/Phoenix            | Excipial <sup>®</sup> almond oil ointment | T041              | 1       |
| Galderma/Phoenix            | Excipial <sup>®</sup> almond oil ointment | 8774005           | 1       |
| Galderma/Phönix             | Excipial <sup>®</sup> almond oil ointment | R043              | 1       |
| Galderma/Phönix             | Excipial <sup>®</sup> almond oil ointment | S021              | 3       |
| Galderma/Phönix             | Excipial <sup>®</sup> almond oil ointment | 50239             | 3       |
| Galderma/Phönix             | Excipial <sup>®</sup> almond oil ointment | 8774007           | 1       |
| Galderma/Phönix             | Excipial <sup>®</sup> almond oil ointment | 9774002           | 1       |
| Galderma-Spirig             | Excipial <sup>®</sup> almond oil ointment | V042-20171127Ma12 | 1       |
| Noweda                      | Excipial <sup>®</sup> almond oil ointment | 8774004           | 1       |
| Noweda                      | Excipial <sup>®</sup> almond oil ointment | 9774003           | 1       |
| Noweda                      | Excipial <sup>®</sup> almond oil ointment | 9774005           | 2       |
| Phoenix                     | Excipial <sup>®</sup> almond oil ointment | LOTN022           | 2       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | M032              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | LOTM023           | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | N031              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | N032              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | M023              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | R012              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | S032              | 1       |
| Spirig                      | Excipial <sup>®</sup> almond oil ointment | S011              | 1       |

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| Supplier                  | Substance                                 | Batch   | Spectra |
|---------------------------|-------------------------------------------|---------|---------|
| Spirig / Galderma / Anzag | Excipial <sup>®</sup> almond oil ointment | V061    | 1       |
| Spirig / Gehe             | Excipial <sup>®</sup> almond oil ointment | LOTN022 | 1       |
| Spirig /Noweda            | Excipial <sup>®</sup> almond oil ointment | R012    | 1       |
| Spirig /Noweda            | Excipial <sup>®</sup> almond oil ointment | r021    | 1       |
| Spirig Pharma AG/Noweda   | Excipial <sup>®</sup> almond oil ointment | 50239   | 1       |
| Spirig Pharma/Nowed       | Excipial <sup>®</sup> almond oil ointment | N022    | 1       |
| Spirig/AHD                | Excipial <sup>®</sup> almond oil ointment | N011    | 1       |
| Spirig/Noweda             | Excipial <sup>®</sup> almond oil ointment | R043    | 1       |
| Spirig/Phönix             | Excipial <sup>®</sup> almond oil ointment | N031    | 1       |
| Spirig/Sanacorp           | Excipial <sup>®</sup> almond oil ointment | LOTN011 | 1       |

- 9243 spectra from 772 *Apo-Ident* customers from a total of 3648 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<sup>®</sup> 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<sup>®</sup> 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 50            | 2              | 9243          |

The substance/substance group *Excipial<sup>®</sup> 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7991 %) | 96.1538 % (> 90.3846 %)  |

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

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

Where the number of spectra does 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<sup>®</sup> 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<br>main model | Distance in<br>second-stage model |
|---------------------------|---------------------------|-----------------------------------|
| Balm Bio Nature           | 11.68                     | —                                 |
| Argan oil                 | 18.00                     | —                                 |
| Wax ointment (stabilised) | 43.54                     | —                                 |
| White paraffin oil        | 53.99                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30720     | 30720                  | 0.00                            | 30.91                              |
| 31090     | 31090                  | 0.00                            | 24.82                              |
| 31278     | 31278                  | 0.00                            | 25.79                              |
| 31757     | 31757                  | 0.00                            | 23.05                              |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Fat ointments</b>                                            |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30881-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany |

### Relevant substance names

Fat ointments; Asche Basis<sup>®</sup> fat ointment; Cottonwood ointment; Deumavan<sup>®</sup> protection ointment neutral; Marjoram ointment; Neribas<sup>®</sup> fat ointment; Protegin<sup>®</sup> 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 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Fat ointments             | 21     | 16     | 195    |

## 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 <sup>®</sup> fat... | 23014A   | 31013     | 40      | not required |
| Chiesi        | Asche Basis <sup>®</sup> fat... | 41017A   | 31858     | 60      | not required |
| Chiesi        | Asche Basis <sup>®</sup> 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 <sup>®</sup> protec... | 41920120 | 35069     | 40      | not required |
| Kaymogyn GmbH | Deumavan <sup>®</sup> 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 <sup>®</sup> fat oin... | 32032C   | 31489     | 40      | not required |
| Jenapharm     | Neribas <sup>®</sup> fat oin... | YY00K7C  | 31872     | 60      | not required |
| Jenapharm     | Neribas <sup>®</sup> fat oin... | YY01TF2  | 33986     | 40      | not required |
| Caelo         | Protegin <sup>®</sup> XN        | 13081901 | 31112     | 40      | not required |
| Caelo         | Protegin <sup>®</sup> XN        | 13344402 | 31475     | 40      | not required |
| Caelo         | Protegin <sup>®</sup> XN        | 17258703 | 33921     | 40      | not required |

## Validation samples

A total of 54 961 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.
- 23 825 spectra from a total of 488 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.

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

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

Samples from batches of which no spectra have been included in the database structure are considered as independent samples. The number of batches from which independent samples supplied *Type B* spectra for validation is shown below, representing the number of independent *Type B* samples. Samples, of which some of the spectra have been included in the database structure and other spectra in the validation, are marked with a <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>®</sup> 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 <sup>®</sup> fat ointment           | YY011K0          | 32764     | 40      |
| Jenapharm     | Neribas <sup>®</sup> fat ointment           | YY019KR          | 33290     | 40      |
| Caelo         | Protegin <sup>®</sup> XN                    | 161645           | 32340     | 40      |
| Chiesi        | Asche Basis <sup>®</sup> fat ointment       | 53021A           | 32716     | 40      |
| Chiesi        | Asche Basis <sup>®</sup> fat ointment       | 53021A           | 32925     | 40      |

- 20 201 spectra from a total of 434 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.

- 725 spectra from 238 *Apo-Ident* customers from 207 batches from the substance/substance group *Fat ointments*.
- Among them are spectra of independent samples from 194 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 <sup>®</sup> fat ointment | 73025A | 1       |
| Caesar Loretz GmbH | Asche Basis <sup>®</sup> fat ointment | 73025A | 2       |
| Chiese             | Asche Basis <sup>®</sup> fat ointment | 33016A | 1       |

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| Supplier        | Substance                             | Batch            | Spectra |
|-----------------|---------------------------------------|------------------|---------|
| Chiese          | Asche Basis <sup>®</sup> fat ointment | 63023A           | 1       |
| Chiesi          | Asche Basis <sup>®</sup> fat ointment | 63023A           | 1       |
| Chiesi          | Asche Basis <sup>®</sup> fat ointment | 51020A           | 1       |
| Chiesi          | Asche Basis <sup>®</sup> fat ointment | 81026A           | 1       |
| Chiesi          | Asche Basis <sup>®</sup> fat ointment | 82027A           | 1       |
| Chiesi          | Asche Basis <sup>®</sup> fat ointment | 84028A           | 1       |
| CHiesi          | Asche Basis <sup>®</sup> fat ointment | 41018A           | 3       |
| Chiesi/ Noweda  | Asche Basis <sup>®</sup> fat ointment | 82027A           | 1       |
| Chiesi/Gehe     | Asche Basis <sup>®</sup> fat ointment | 51020A           | 1       |
| Chiesi/Gehe     | Asche Basis <sup>®</sup> 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                     | 8031304          | 1       |
| Caelo           | Marjoram ointment                     | 5322500          | 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                     | 16068801         | 3       |
| Caelo           | Marjoram ointment                     | 16068602         | 5       |
| Caelo           | Marjoram ointment                     | 16257602         | 5       |
| Caelo           | Marjoram ointment                     | 16257502         | 3       |
| Caelo           | Marjoram ointment                     | 17071001         | 3       |
| Caelo           | Marjoram ointment                     | 17071101         | 9       |
| Caelo           | Marjoram ointment                     | 17302401         | 6       |
| Caelo           | Marjoram ointment                     | 19033001         | 13      |
| Caelo           | Marjoram ointment                     | 1903301          | 1       |
| Caelo           | Marjoram ointment                     | 18251603         | 1       |
| Caelo           | Marjoram ointment                     | 19033101         | 1       |
| Caelo           | Marjoram ointment                     | 19033120         | 1       |
| Caelo           | Marjoram ointment                     | 13307102         | 6       |
| 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         | 4       |
| Caelo           | Marjoram ointment                     | 13028302         | 3       |
| Caelo           | Marjoram ointment                     | 19115103         | 2       |
| Caelo           | Marjoram ointment                     | 1225402          | 1       |

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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         | 10      |
| Caelo                        | Marjoram ointment | 13383001         | 1       |
| Caelo                        | Marjoram ointment | 13e10-t04-003550 | 1       |
| Caelo                        | Marjoram ointment | 14332101         | 9       |
| Caelo                        | Marjoram ointment | 16068701         | 5       |
| Caelo                        | Marjoram ointment | 19033102         | 15      |
| Caelo                        | Marjoram ointment | 12295402         | 6       |
| Caelo                        | Marjoram ointment | 16068901         | 8       |
| Caelo                        | Marjoram ointment | 14002101         | 16      |
| Caelo                        | Marjoram ointment | 16K07-T20-038496 | 1       |
| Caelo                        | Marjoram ointment | 18190101         | 5       |
| Caelo                        | Marjoram ointment | 18190001         | 11      |
| Caelo                        | Marjoram ointment | 20000281001      | 3       |
| Caelo                        | Marjoram ointment | 1513E-02536      | 1       |
| Caecolo                      | Marjoram ointment | 14090002         | 1       |
| Caecolo                      | Marjoram ointment | 1539402          | 1       |
| Caesar & Lorenz Sanacorp     | Marjoram ointment | 19033102         | 1       |
| Caesar & Loretz GmbH         | Marjoram ointment | 19033001         | 1       |
| Caesar & Loretz GmbH/Je. . . | Marjoram ointment | 20003044001      | 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 | 3       |
| Fagron                       | Marjoram ointment | 14a07-T04009079  | 1       |
| Fagron                       | Marjoram ointment | T03-0691303      | 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 | 18190102         | 5       |
| Gehe                         | Marjoram ointment | 19033001         | 1       |
| Caelo                        | Marjoram ointment | 17302402         | 2       |

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| Supplier                     | Substance                         | Batch     | Spectra |
|------------------------------|-----------------------------------|-----------|---------|
| Caelo                        | Marjoram ointment                 | 18050901  | 6       |
| Caelo                        | Marjoram ointment                 | 12123101  | 2       |
| Caelo                        | Marjoram ointment                 | 13028301  | 2       |
| Caelo                        | Marjoram ointment                 | 13382901  | 1       |
| Fagron                       | Marjoram ointment                 | 19G04-T03 | 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       |
| Caelo                        | Marjoram ointment                 | 19115102  | 1       |
| 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 <sup>®</sup> fat ointment | YY016LP   | 2       |
| Alliance Healthcare          | Neribas <sup>®</sup> fat ointment | YY0431T   | 1       |
| BAYER/Phönix WE:26.04.1. . . | Neribas <sup>®</sup> fat ointment | YY011K0   | 1       |
| Caelo                        | Neribas <sup>®</sup> fat ointment | yy00k7C   | 1       |
| GP Grenzach Produktions. . . | Neribas <sup>®</sup> fat ointment | YY00K7C   | 1       |
| Hedinger/Sanacorp            | Neribas <sup>®</sup> fat ointment | YY01TF2   | 2       |
| Jenapharm                    | Neribas <sup>®</sup> fat ointment | YY016LP   | 1       |
| Jenapharm                    | Neribas <sup>®</sup> fat ointment | YY0282F   | 1       |
| Jenapharm / Fiebig           | Neribas <sup>®</sup> fat ointment | YY01TF2   | 1       |
| Jenapharm /Gehe              | Neribas <sup>®</sup> fat ointment | YY0282F   | 1       |
| Jenapharm/                   | Neribas <sup>®</sup> fat ointment | YY011K0   | 1       |
| Jenapharm/AHCA               | Neribas <sup>®</sup> fat ointment | YY0282F   | 2       |
| Jenapharm/AHCA               | Neribas <sup>®</sup> fat ointment | YY02L7L   | 2       |
| Jenapharm/Ahd                | Neribas <sup>®</sup> fat ointment | YYo11Ko   | 1       |
| Jenapharm/Anzag              | Neribas <sup>®</sup> fat ointment | YY0282F   | 1       |
| Jenapharm/Krieger            | Neribas <sup>®</sup> fat ointment | YY0282F   | 3       |
| Jenapharm/Krieger            | Neribas <sup>®</sup> fat ointment | YY02L7L   | 3       |
| Jenapharm/Noweda             | Neribas <sup>®</sup> fat ointment | YY01TF2   | 1       |
| Jenapharm/Phönix             | Neribas <sup>®</sup> fat ointment | YY00K7C   | 1       |
| Jenapharm/Phönix             | Neribas <sup>®</sup> fat ointment | YY0282F   | 1       |
| Leo Pharma                   | Neribas <sup>®</sup> fat ointment | YY0431T   | 1       |
| LeoPharma/Krieger            | Neribas <sup>®</sup> fat ointment | YY04F1L   | 1       |
| LeoPharma/Phönix             | Neribas <sup>®</sup> fat ointment | YY0431T   | 1       |
| Noweda                       | Neribas <sup>®</sup> fat ointment | YY0282F   | 4       |
| Phoenix                      | Neribas <sup>®</sup> fat ointment | YY00K7C   | 1       |

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| <b>Supplier</b>            | <b>Substance</b>                  | <b>Batch</b> | <b>Spectra</b> |
|----------------------------|-----------------------------------|--------------|----------------|
| Phoenix WE 24.04.17 -7,... | Neribas <sup>®</sup> fat ointment | YY019KR      | 1              |
| PhönixWE:18.01.2017 E...   | Neribas <sup>®</sup> fat ointment | YY016LP      | 1              |
| Römerapo.                  | Neribas <sup>®</sup> fat ointment | YY01TF2      | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 3091208      | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 11196702     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 11022403     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 12229201     | 5              |
| Caelo                      | Protegin <sup>®</sup> XN          | 11196802     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 8031305      | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 12229211     | 5              |
| Caelo                      | Protegin <sup>®</sup> XN          | 25061301     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 12229210     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 12229209     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081903     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081908     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 6012014A     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 20011402     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081904     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13091906     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081907     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220204     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220203     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14341301     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 26031509     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220208     | 4              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220206     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 15252703     | 5              |
| Caelo                      | Protegin <sup>®</sup> XN          | 15252702     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026703     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026707     | 6              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026706     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164505     | 5              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164503     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 17256702     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 17258707     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059501     | 10             |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059511     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 19109002     | 11             |
| Caelo                      | Protegin <sup>®</sup> XN          | 20001749001  | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 20001749003  | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 19109001     | 4              |
| Caelo                      | Protegin <sup>®</sup> XN          | 11196805     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 20001749005  | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026704     | 4              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081902     | 3              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220209     | 4              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026702     | 5              |
| Caelo                      | Protegin <sup>®</sup> XN          | 20001749007  | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081906     | 6              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026709     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164504     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164501     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 14341302     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 11196801     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 13344401     | 6              |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164506     | 2              |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059507     | 7              |
| Caelo                      | Protegin <sup>®</sup> XN          | 17258705     | 1              |
| Caelo                      | Protegin <sup>®</sup> XN          | 17258708     | 1              |
| Fagron                     | Protegin <sup>®</sup> XN          | 18059501     | 1              |

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| Supplier                   | Substance                         | Batch       | Spectra |
|----------------------------|-----------------------------------|-------------|---------|
| Caelo                      | Protegin <sup>®</sup> XN          | 14220202    | 5       |
| Caelo                      | Protegin <sup>®</sup> XN          | 16026701    | 6       |
| Caelo                      | Protegin <sup>®</sup> XN          | 1805907     | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059505    | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059509    | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059502    | 10      |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059503    | 2       |
| Caelo                      | Protegin <sup>®</sup> XN          | 18059512    | 4       |
| Caelo                      | Protegin <sup>®</sup> XN          | 19109003    | 2       |
| Caelo                      | Protegin <sup>®</sup> XN          | 19110202    | 13      |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081905    | 11      |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220201    | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 1805901     | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 19110201    | 7       |
| Caelo                      | Protegin <sup>®</sup> XN          | 191092002   | 4       |
| Caesar & Loretz            | Protegin <sup>®</sup> XN          | 19109001    | 1       |
| Caesar & Loretz            | Protegin <sup>®</sup> XN          | 19110201    | 1       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 18059511    | 1       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 18059512    | 3       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 19109001    | 1       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 18059501    | 1       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 18059507    | 1       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 19109002    | 5       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 19110202    | 7       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 20001749001 | 2       |
| Caesar & Loretz GmbH       | Protegin <sup>®</sup> XN          | 20001749003 | 1       |
| Caesar & Loretz GmbH / ... | Protegin <sup>®</sup> XN          | 19110202    | 2       |
| Caesar & Loretz GmbH / ... | Protegin <sup>®</sup> XN          | 19110201    | 1       |
| Caesar & Loretz GmbH/ N... | Protegin <sup>®</sup> XN          | 18059507    | 1       |
| Fagron                     | Protegin <sup>®</sup> XN          | 18059507    | 1       |
| Gehe                       | Protegin <sup>®</sup> XN          | 12229201    | 1       |
| Gehe                       | Protegin <sup>®</sup> XN          | 12229211    | 1       |
| Gehe                       | Protegin <sup>®</sup> XN          | 16026701    | 2       |
| GEHE                       | Protegin <sup>®</sup> XN          | 18059507    | 1       |
| Hedinger/Phönix            | Protegin <sup>®</sup> XN          | 18059501    | 1       |
| Ichthyol-Gesellschaft      | Protegin <sup>®</sup> XN          | 17258703    | 1       |
| Kehr                       | Protegin <sup>®</sup> XN          | 1805607     | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 16164502    | 2       |
| Klenk                      | Protegin <sup>®</sup> XN          | 18059502    | 1       |
| krieger                    | Protegin <sup>®</sup> XN          | 19110202    | 1       |
| Phoenix                    | Protegin <sup>®</sup> XN          | 19110202    | 1       |
| Phönix                     | Protegin <sup>®</sup> XN          | 11196706    | 1       |
| Phönix                     | Protegin <sup>®</sup> XN          | 13081901    | 3       |
| Phönix                     | Protegin <sup>®</sup> XN          | 16026707    | 1       |
| PHÖNIX                     | Protegin <sup>®</sup> XN          | 18059501    | 1       |
| Phönix 12.03.2013          | Protegin <sup>®</sup> XN          | 12229205    | 1       |
| Phönix, 07.11.13           | Protegin <sup>®</sup> XN          | 12229210    | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 14220205    | 6       |
| Caelo                      | Marjoram ointment                 | 12123001    | 7       |
| Caelo                      | Marjoram ointment                 | 14089901    | 8       |
| Jenapharm                  | Neribas <sup>®</sup> fat ointment | YY01TF2     | 1       |
|                            | Protegin <sup>®</sup> XN          | 2711E-03598 | 1       |
| Caelo                      | Protegin <sup>®</sup> XN          | 13344402    | 11      |
| Caelo                      | Protegin <sup>®</sup> XN          | 13081901    | 4       |
| Caelo                      | Protegin <sup>®</sup> XN          | 17258703    | 3       |
| Euro OTC                   | Protegin <sup>®</sup> XN          |             | 1       |

- 8570 spectra from 750 *Apo-Ident* customers from a total of 3468 batches from a further 145 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 *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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 880           | 0              | 23 825        |
| <b>Type B</b> | 0              | 760           | 0              | 20 161        |
| <b>Type C</b> | 0              | 708           | 17             | 8570          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.3182 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 99.2105 %) |
| <b>Type C</b> | 100.0000 % (> 98.7980 %) | 97.6552 % (> 97.2414 %)  |

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

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

Where the number of spectra does 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           | 12.31                  | —                              |
| Wax ointment (stabilised)    | 28.26                  | —                              |
| Lygal® head ointment N 3%    | 31.08                  | —                              |
| Salicylic white paraffin 10% | 59.04                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30881     | 30881               | 0.00                         | 33.49                           |
| 30926     | 30926               | 0.00                         | 39.52                           |
| 31013     | 31013               | 0.00                         | 36.82                           |
| 31112     | 31112               | 0.00                         | 38.27                           |
| 31443     | 31443               | 0.00                         | 36.31                           |
| 31475     | 31475               | 0.00                         | 39.65                           |
| 31489     | 31489               | 0.00                         | 43.73                           |
| 31858     | 31858               | 0.00                         | 45.21                           |
| 31872     | 31872               | 0.00                         | 47.83                           |
| 32473     | 32473               | 0.00                         | 31.06                           |
| 33130     | 33130               | 0.00                         | 30.77                           |
| 33131     | 33131               | 0.00                         | 32.53                           |
| 33634     | 33634               | 0.00                         | 42.44                           |
| 33921     | 33921               | 0.00                         | 38.16                           |
| 33986     | 33986               | 0.00                         | 42.79                           |
| 34783     | 34783               | 0.00                         | 38.75                           |
| 34963     | 34963               | 0.00                         | 33.80                           |
| 34966     | 34966               | 0.00                         | 34.59                           |
| 34967     | 34967               | 0.00                         | 33.45                           |
| 35069     | 35069               | 0.00                         | 22.27                           |
| 35071     | 35071               | 0.00                         | 23.01                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Fenistil® Gel**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31045-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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      |

- 20 881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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 <sup>®</sup> cream lotion pH 5        | 16.32                  | —                              |
| Sebexol <sup>®</sup> basic pH 5 formula basis | 21.45                  | —                              |
| SyrSpend <sup>®</sup> SF pH4 cherry aroma     | 22.42                  | —                              |
| Hans Karrer Hydrocream MicroSilver            | 23.21                  | —                              |
| Aloe vera gel, 10x concentrated               | 26.44                  | —                              |
| Bepanthen <sup>®</sup> solution               | 27.54                  | —                              |
| Retterspitz external                          | 27.85                  | —                              |
| SyrSpend <sup>®</sup> SF pH4 aroma free       | 30.11                  | —                              |
| Water                                         | 32.24                  | —                              |
| Wofacutan wash lotion                         | 33.90                  | —                              |
| Aloe Vera gel, 1:1                            | 34.94                  | —                              |
| Excipial <sup>®</sup> U Hydrolotio            | 35.19                  | —                              |
| Dimeticone ointment 10% SR                    | 36.82                  | —                              |
| Abitima <sup>®</sup> clinic face cream        | 50.26                  | —                              |

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                         | 19.21                           |
| 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 2.4-2021-02

Validated substance/substance group **Fennel oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31140-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 74            | 6              | 20 881        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 92.5000 % (> 88.7500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------------|---------------------------|-----------------------------------|
| Anise oil, organic | 15.73                     | —                                 |
| Thuja oil          | 77.83                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31140     | 31140                  | 0.00                            | 84.97                              |
| 31693     | 31693                  | 0.00                            | 84.84                              |
| 32795     | 32795                  | 0.00                            | 20.07                              |

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 2.4-2021-02

Validated substance/substance group **Ginger oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30451-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------------------|---------------------------|-----------------------------------|
| Citrus oil               | 17.79                     | —                                 |
| Cedar wood oil           | 18.83                     | —                                 |
| Hyssop oil               | 20.10                     | —                                 |
| Vetiver bourbon oil      | 23.61                     | —                                 |
| Marjoram oil             | 24.64                     | —                                 |
| Angelica root oil        | 26.01                     | —                                 |
| Myrtle oil               | 27.89                     | —                                 |
| Lemon grass oil          | 30.28                     | —                                 |
| Immortelle oil           | 33.30                     | —                                 |
| Cypress oil              | 36.06                     | —                                 |
| Carrot seed oil          | 37.11                     | —                                 |
| Spearmint oil            | 38.21                     | —                                 |
| Yarrow oil               | 39.42                     | —                                 |
| Spruce needle oil        | 41.25                     | —                                 |
| Cumin oil                | 44.86                     | —                                 |
| Frankincense oil         | 45.79                     | —                                 |
| Patchouli oil            | 46.83                     | —                                 |
| Silver fir oil           | 47.41                     | —                                 |
| Matricaria oil, morrocan | 51.31                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30958     | 30958                  | 0.00                            | 20.10                              |
| 31142     | 31142                  | 0.00                            | 18.83                              |
| 32270     | 32270                  | 0.00                            | 29.03                              |
| 34407     | 34407                  | 0.00                            | 30.63                              |

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 2.4-2021-02

Validated substance/substance group **Grapefruit oil organic / Orange oil / Blood orange oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30960-2021-06-11  
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/substance group                              | Type A | Type B | Type C |
|--------------------------------------------------------|--------|--------|--------|
| Grapefruit oil organic / Orange oil / Blood orange oil | 8      | 12     | 33     |

## 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 54 961 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.
- 24 245 spectra from a total of 501 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 490 spectra from a total of 439 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 | 31564-120540    | 1       |
| Taoasis          | Grapefruit oil, organic | 40038-123110    | 1       |
| Taoasis          | Grapefruit oil, organic | 44040A-127409   | 1       |
| Taoasis          | Grapefruit oil, organic | 44040A-124467   | 1       |
| Taoasis          | Grapefruit oil, organic | 46701-128853    | 1       |
| Taoasis          | Grapefruit oil, organic | 44040A-124468   | 1       |
| Taoasis          | Grapefruit oil, organic | 47037-958       | 1       |
| Taoasis          | Grapefruit oil, organic | 47037-1144      | 2       |
| 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              | 298756          | 1       |
| Bombastus        | Orange oil              | 302428          | 1       |
| Taoasis          | Orange oil              | 140129-116983   | 1       |
| Taoasis          | Orange oil              | 140129-118141   | 1       |
| Taoasis          | Orange oil              | 140129-118790   | 1       |
| Taoasis          | Orange oil              | 42861A-121691   | 1       |
| Taoasis          | Orange oil              | 42861A-122532   | 1       |
| Taoasis          | Orange oil              | 140129-118420   | 1       |
| Taoasis          | Orange oil              | 122650-123643   | 1       |
| Taoasis          | Orange oil              | 43829C-125351   | 1       |
| Taoasis          | Orange oil              | 43829C-124155   | 1       |
| Taoasis          | Orange oil              | 44583A-128241   | 1       |

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| Supplier        | Substance  | Batch         | Spectra |
|-----------------|------------|---------------|---------|
| Taoasis         | Orange oil | 45451A-1178   | 1       |
| Taoasis         | Orange oil | 45451A-128935 | 1       |
| Taoasis         | Orange oil | 45441A-1035   | 1       |
| Taoasis         | Orange oil | 11855A-3824   | 1       |
| Taoasis         | Orange oil | 6193          | 1       |
| Taoasis/Gehe    | Orange oil | 497J09        | 1       |
| Taoasis/Taoasis | Orange oil | 44583A-127488 | 1       |

- 9261 spectra from 771 *Apo-Ident* customers from a total of 3642 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              | 24 245        |
| Type B | 0              | 471           | 0              | 20 490        |
| Type C | 0              | 34            | 0              | 9261          |

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 % (> 99.9602 %) | 100.0000 % (> 98.6957 %) |
| Type B | 100.0000 % (> 99.9453 %) | 100.0000 % (> 98.7261 %) |
| Type C | 100.0000 % (> 98.7998 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Citric oil          | 16.89                     | —                                 |
| Mandarin oil, green | 43.93                     | —                                 |
| Lime oil            | 58.19                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30960     | 30960                  | 0.00                            | 43.33                              |
| 31634     | 31634                  | 0.00                            | 41.52                              |
| 31679     | 31679                  | 0.00                            | 45.32                              |
| 31781     | 31781                  | 0.00                            | 46.09                              |
| 31853     | 31853                  | 0.00                            | 36.24                              |
| 33759     | 33759                  | 0.00                            | 43.77                              |
| 33761     | 33761                  | 0.00                            | 43.15                              |
| 33805     | 33805                  | 0.00                            | 44.23                              |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Hydrophilic ointments</b>                                    |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30634-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany |

### Relevant substance names

Hydrophilic ointments; Abitima<sup>®</sup> clinic body cream; Abitima<sup>®</sup> clinic face cream; Allergika<sup>®</sup> Base cream; Asche Basis<sup>®</sup> cream; Asche Basis<sup>®</sup> lotion; Base cream Taoasis; Dermatest base ointment; Dermatop<sup>®</sup> base cream; DMS<sup>®</sup> base cream classic; DMS<sup>®</sup> base cream high classic; DMS<sup>®</sup> base cream high classic plus; Eucerinum O/W basis; Eucerinum W/O basis; Excipial<sup>®</sup> hydro cream; Excipial<sup>®</sup> lipo cream; Excipial<sup>®</sup> U Lipolotio; Excipial<sup>®</sup> U10 Lipolotio; Fabitop<sup>®</sup> base cream; Hans Karrer Lipocream MicroSilver; Hans Karrer Lipolotion MicroSilver; Linola<sup>®</sup> body milk; Lipoderm<sup>®</sup> lotion; Neribas<sup>®</sup> cream; Neuroderm<sup>®</sup> care lotion; Neuroderm<sup>®</sup> 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Hydrophilic ointments     | 75     | 40     | 961    |

## 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 <sup>®</sup> clinic ... | 110712      | 31058     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 051112      | 31061     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 070915      | 32997     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 331017      | 33969     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 46820       | 30845     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 161464      | 33793     | 40      | not required |
| Actavis          | Abitima <sup>®</sup> clinic ... | 170180      | 34360     | 40      | not required |
| Allergika        | Allergika <sup>®</sup> Base ... | 11/082022   | 33668     | 40      | not required |
| Allergika        | Allergika <sup>®</sup> Base ... | 10/082022   | 33669     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> cream  | 03117A      | 30713     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> cream  | 22197A      | 30775     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> cream  | 24220A      | 31085     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> lot... | 21042A      | 30828     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> lot... | 24049A      | 31068     | 40      | not required |
| Chiesi           | Asche Basis <sup>®</sup> 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 |
| 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 <sup>®</sup> base c... | 3F031A      | 31234     | 40      | not required |
| Sanofi aventis   | Dermatop <sup>®</sup> base c... | 5F056A      | 32177     | 40      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L026G13     | 31307     | 40      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L034H15     | 31869     | 60      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L003H16     | 32916     | 40      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L009K17     | 33968     | 40      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L010K13     | 31236     | 70      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L032A14     | 31308     | 40      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L041K15     | 31870     | 60      | not required |
| Koko             | DMS <sup>®</sup> base cream ... | L014L13     | 31309     | 40      | not required |
| Koko             | DMS <sup>®</sup> 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 <sup>®</sup> hydro ... | I013        | 30725     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> hydro ... | N013        | 31089     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> hydro ... | T052        | 33208     | 40      | not required |
| Galderma Labo... | Excipial <sup>®</sup> lipo c... | V051        | 33636     | 40      | not required |

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| Supplier         | Substance                       | Batch     | Sample ID | Spectra | Certificate  |
|------------------|---------------------------------|-----------|-----------|---------|--------------|
| Spirig Pharma    | Excipial <sup>®</sup> lipo c... | I011      | 30726     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> lipo c... | N017      | 31088     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> lipo c... | R011      | 31520     | 60      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> lipo c... | T081      | 33207     | 40      | not required |
| Galderma Labo... | Excipial <sup>®</sup> U Lipo... | T122      | 33270     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U Lipo... | M042      | 30732     | 60      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U Lipo... | N031      | 31067     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U Lipo... | N085      | 31280     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U10 Li... | M021      | 30733     | 60      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U10 Li... | N025      | 31066     | 40      | not required |
| Spirig Pharma    | Excipial <sup>®</sup> U10 Li... | N047      | 31281     | 40      | not required |
| Fontapharm       | Fabitol <sup>®</sup> base cr... | 6RWW2     | 31082     | 40      | not required |
| Fontapharm       | Fabitol <sup>®</sup> base cr... | GWWL3     | 31576     | 60      | not required |
| Fontapharm       | Fabitol <sup>®</sup> 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 <sup>®</sup> body milk   | 433240    | 31511     | 60      | not required |
| Dr. Wolff        | Linola <sup>®</sup> body milk   | 511750    | 31874     | 60      | not required |
| Dr. Wolff        | Linola <sup>®</sup> body milk   | 707930    | 34043     | 40      | not required |
| Spirig Pharma    | Lipoderm <sup>®</sup> lotion    | K057      | 30635     | 40      | not required |
| Spirig Pharma    | Lipoderm <sup>®</sup> lotion    | M065      | 31072     | 40      | not required |
| Spirig Pharma    | Lipoderm <sup>®</sup> lotion    | R023      | 31535     | 60      | not required |
| Intendis         | Neribas <sup>®</sup> cream      | 21076A    | 30634     | 40      | not required |
| Intendis         | Neribas <sup>®</sup> cream      | 21076A    | 31050     | 40      | not required |
| Intendis         | Neribas <sup>®</sup> cream      | 21076A    | 31095     | 40      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> care ... | S041204.1 | 31070     | 40      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> care ... | S031505.1 | 31772     | 60      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> care ... | S071706.1 | 34044     | 40      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> moist... | S041214.1 | 30722     | 40      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> moist... | S021307.1 | 31102     | 40      | not required |
| Infectopharm     | Neuroderm <sup>®</sup> moist... | S101428.1 | 31761     | 60      | not required |

## Validation samples

A total of 54 961 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.
- 21 195 spectra from a total of 437 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>®</sup> clinic body cream      | 072013      | 30736     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic body cream      | 040116      | 32999     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic body cream      | 150818      | 34363     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic face cream      | 158584      | 32179     | 40      |
| Allergika                  | Allergika <sup>®</sup> Base cream           | 09/072022   | 33670     | 40      |
| Chiesi                     | Asche Basis <sup>®</sup> cream              | 63351A      | 32928     | 40      |
| Chiesi                     | Asche Basis <sup>®</sup> cream              | 63354A      | 33435     | 40      |
| Chiesi                     | Asche Basis <sup>®</sup> 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 <sup>®</sup> base cream            | 5F057A      | 32717     | 40      |
| Sanofi aventis             | Dermatop <sup>®</sup> base cream            | 7F069A      | 33966     | 40      |
| Koko                       | DMS <sup>®</sup> base cream classic         | L003E16     | 32788     | 40      |
| Koko                       | DMS <sup>®</sup> base cream high classic    | L037K16     | 33433     | 40      |
| Koko                       | DMS <sup>®</sup> base cream high classic... | L018D16     | 32827     | 40      |
| Beiersdorf                 | Eucerinum W/O basis                         | 72630108WA  | 33629     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> hydro cream           | 50235       | 33982     | 40      |
| Galderma Laboratorium G... | Excipial <sup>®</sup> U Lipolotio           | V011        | 33298     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio           | T122        | 33204     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> U10 Lipolotio         | T072        | 33205     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> U10 Lipolotio         | 50393       | 33980     | 40      |
| Fontapharm                 | Fabitol <sup>®</sup> base cream             | GRWW1       | 30835     | 40      |
| Fontapharm                 | Fabitol <sup>®</sup> 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 <sup>®</sup> body milk               | 606430      | 32765     | 40      |
| Dr. Wolff                  | Linola <sup>®</sup> body milk               | 609202      | 33258     | 40      |
| Spirig Pharma              | Lipoderm <sup>®</sup> lotion                | V012        | 33248     | 40      |
| Spirig Pharma              | Lipoderm <sup>®</sup> lotion                | V042        | 33985     | 40      |
| Jenapharm                  | Neribas <sup>®</sup> cream                  | YY01FX3     | 33289     | 40      |
| Jenapharm                  | Neribas <sup>®</sup> cream                  | YY01X64     | 33951     | 40      |
| Infectopharm               | Neuroderm <sup>®</sup> care lotion          | S111514.1   | 32740     | 40      |
| Infectopharm               | Neuroderm <sup>®</sup> care lotion          | S081610.1   | 33286     | 40      |
| Infectopharm               | Neuroderm <sup>®</sup> moisturising cream   | S051612.1   | 32905     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic body cream      | 040116      | 33791     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic face cream      | 158584      | 32723     | 40      |
| Actavis                    | Abitima <sup>®</sup> clinic face cream      | 158584      | 32998     | 40      |
| Chiesi                     | Asche Basis <sup>®</sup> lotion             | 53075A      | 32926     | 40      |
| Taoasis                    | Base cream Taoasis                          | 161124-6322 | 32945     | 40      |
| Koko                       | DMS <sup>®</sup> base cream classic         | L003E16     | 32826     | 40      |

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| Supplier                   | Substance                                 | Batch      | Sample ID | Spectra |
|----------------------------|-------------------------------------------|------------|-----------|---------|
| Koko                       | DMS <sup>®</sup> base cream high classic  | L003H16    | 32789     | 40      |
| Koko                       | DMS <sup>®</sup> 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 <sup>®</sup> hydro cream         | I013       | 30836     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> hydro cream         | N013       | 31277     | 40      |
| Galderma Laboratorium G... | Excipial <sup>®</sup> lipo cream          | V051       | 33637     | 40      |
| Spirig Pharma              | Excipial <sup>®</sup> lipo cream          | N017       | 31276     | 40      |
| Galderma Laboratorium G... | Excipial <sup>®</sup> U Lipolotio         | T122       | 33269     | 40      |
| Infectopharm               | Neuroderm <sup>®</sup> moisturising cream | S051612.1  | 32906     | 40      |

- 18741 spectra from a total of 406 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.

- 2561 spectra from 342 *Apo-Ident* customers from 993 batches from the substance/substance group *Hydrophilic ointments*.
- Among them are spectra of independent samples from 890 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 <sup>®</sup> clinic body cream | 260515       | 2       |
| Abitima                  | Abitima <sup>®</sup> clinic body cream | 52015/051112 | 1       |
| Abitima / Gehe           | Abitima <sup>®</sup> clinic body cream | 251118       | 1       |
| actavis                  | Abitima <sup>®</sup> clinic body cream | 20912        | 2       |
| actavis                  | Abitima <sup>®</sup> clinic body cream | 60513        | 2       |
| actavis                  | Abitima <sup>®</sup> clinic body cream | 140113       | 1       |
| actavis                  | Abitima <sup>®</sup> clinic body cream | 70513        | 1       |
| actavis                  | Abitima <sup>®</sup> clinic body cream | 110517       | 1       |
| Actavis                  | Abitima <sup>®</sup> clinic body cream | 20912        | 1       |
| Actavis                  | Abitima <sup>®</sup> clinic body cream | 31114        | 2       |
| Actavis                  | Abitima <sup>®</sup> clinic body cream | 10915        | 4       |
| Actavis                  | Abitima <sup>®</sup> clinic body cream | 31015        | 2       |
| Actavis                  | Abitima <sup>®</sup> clinic body cream | 32018        | 1       |
| Actavis / Gehe           | Abitima <sup>®</sup> clinic body cream | 110712       | 1       |
| Actavis Deutschland GmbH | Abitima <sup>®</sup> clinic body cream | 350313       | 2       |
| Actavis Deutschland GmbH | Abitima <sup>®</sup> clinic body cream | 31015        | 1       |
| Actavis Deutschland GmbH | Abitima <sup>®</sup> clinic body cream | 121115       | 1       |
| Actavis Group PTC        | Abitima <sup>®</sup> clinic body cream | 260515       | 1       |
| Actavis/                 | Abitima <sup>®</sup> clinic body cream | 21015        | 1       |
| Actavis/ Gehe            | Abitima <sup>®</sup> clinic body cream | 60513        | 1       |
| actavis/ebert            | Abitima <sup>®</sup> clinic body cream | 110712       | 1       |
| actavis/Gehe             | Abitima <sup>®</sup> clinic body cream | 112015       | 1       |
| actavis/Gehe             | Abitima <sup>®</sup> clinic body cream | 110712       | 2       |
| actavis/Gehe             | Abitima <sup>®</sup> clinic body cream | 60513        | 1       |
| Actavis/Gehe             | Abitima <sup>®</sup> clinic body cream | 51112        | 1       |
| Actavis/Gehe             | Abitima <sup>®</sup> clinic body cream | 81013        | 1       |
| Actavis/Noweda           | Abitima <sup>®</sup> clinic body cream | 21015        | 1       |

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| Supplier                   | Substance                              | Batch        | Spectra |
|----------------------------|----------------------------------------|--------------|---------|
| Actavis/Sanacorp           | Abitima <sup>®</sup> clinic body cream | 110712       | 1       |
| APL swift Service/AHD      | Abitima <sup>®</sup> clinic body cream | 251118       | 1       |
| APL swift Service/Sanac... | Abitima <sup>®</sup> clinic body cream | 90118        | 1       |
| APL Swift/ Phö             | Abitima <sup>®</sup> clinic body cream | 131118       | 1       |
| Astellas Pharma            | Abitima <sup>®</sup> clinic body cream | 190213       | 1       |
| Balkanpharma               | Abitima <sup>®</sup> clinic body cream | 90118        | 2       |
| Caelo                      | Abitima <sup>®</sup> clinic body cream | 40116        | 1       |
| GEHE                       | Abitima <sup>®</sup> clinic body cream | 331017       | 2       |
| GEHE                       | Abitima <sup>®</sup> clinic body cream | 100116       | 2       |
| Noweda/Actavis             | Abitima <sup>®</sup> clinic body cream | 90118        | 2       |
| Fagron                     | Abitima <sup>®</sup> clinic body cream | 110517       | 2       |
| Fagron                     | Abitima <sup>®</sup> clinic body cream | 241118       | 1       |
| Fagron                     | Abitima <sup>®</sup> clinic body cream | 251118       | 2       |
| Puren                      | Abitima <sup>®</sup> clinic body cream | 251118       | 1       |
| Puren Ph./Gehe             | Abitima <sup>®</sup> clinic body cream | 131118       | 1       |
| Puren Pharm/Phoenix        | Abitima <sup>®</sup> clinic body cream | 241118       | 2       |
| Puren Pharm/Phoenix        | Abitima <sup>®</sup> clinic body cream | 120119       | 1       |
| Puren Pharm/Phoenix        | Abitima <sup>®</sup> clinic body cream | 130319       | 1       |
| Puren Pharm/Phönix         | Abitima <sup>®</sup> clinic body cream | 251118       | 10      |
| Puren Pharm/Phönix         | Abitima <sup>®</sup> clinic body cream | 1311118      | 1       |
| Puren Pharm/Phönix         | Abitima <sup>®</sup> clinic body cream | 261118       | 12      |
| Puren Pharma               | Abitima <sup>®</sup> clinic body cream | 120319       | 1       |
| Puren Pharma / Phönix      | Abitima <sup>®</sup> clinic body cream | 251118       | 2       |
| Puren Pharma GmbH          | Abitima <sup>®</sup> clinic body cream | 131118       | 2       |
| Puren Pharma GmbH          | Abitima <sup>®</sup> clinic body cream | 13118        | 1       |
| PUREN Pharma GmbH &CoKG... | Abitima <sup>®</sup> clinic body cream | 90118        | 1       |
| Puren Pharma GmbH / Kehr   | Abitima <sup>®</sup> clinic body cream | 131118       | 2       |
| Puren Pharma GmbH / Lie... | Abitima <sup>®</sup> clinic body cream | 90118        | 2       |
| Puren Pharma/Noweda        | Abitima <sup>®</sup> clinic body cream | 90118        | 1       |
| Puren/Phoenix              | Abitima <sup>®</sup> clinic body cream | 130118       | 1       |
| Puren/Phoenix              | Abitima <sup>®</sup> clinic body cream | 261118       | 1       |
| Puren/Phoenix              | Abitima <sup>®</sup> clinic body cream | 130319       | 1       |
| Roche/AHD                  | Abitima <sup>®</sup> clinic body cream | 142620       | 1       |
| Sanacorp                   | Abitima <sup>®</sup> clinic body cream | 210612       | 1       |
| Sanacorp                   | Abitima <sup>®</sup> clinic body cream | 70512        | 1       |
| Sanacorp                   | Abitima <sup>®</sup> clinic body cream | 51112        | 1       |
| Sanacorp                   | Abitima <sup>®</sup> clinic body cream | 12015/110/12 | 1       |
| Sanacorp                   | Abitima <sup>®</sup> clinic body cream | 140113       | 1       |
| actavis                    | Abitima <sup>®</sup> clinic face cream | 148496       | 2       |
| actavis                    | Abitima <sup>®</sup> clinic face cream | 148495       | 1       |
| actavis                    | Abitima <sup>®</sup> clinic face cream | 150202       | 1       |
| actavis                    | Abitima <sup>®</sup> clinic face cream | 150203       | 2       |
| Actavis                    | Abitima <sup>®</sup> clinic face cream | 160670       | 1       |
| Actavis / Anzag            | Abitima <sup>®</sup> clinic face cream | 148024       | 1       |
| Actavis / Anzag            | Abitima <sup>®</sup> clinic face cream | 148503       | 1       |
| Actavis / Anzag            | Abitima <sup>®</sup> clinic face cream | 150237       | 1       |
| Actavis / Gehe             | Abitima <sup>®</sup> clinic face cream | 161904       | 3       |
| Actavis / Noweda           | Abitima <sup>®</sup> clinic face cream | 142371       | 1       |
| actavis group              | Abitima <sup>®</sup> clinic face cream | 161468       | 1       |
| Actavis/Gehe               | Abitima <sup>®</sup> clinic face cream | 148495       | 1       |
| Actavis/GEHE               | Abitima <sup>®</sup> clinic face cream | 148051       | 1       |
| Actavis/Noweda             | Abitima <sup>®</sup> clinic face cream | 161423       | 1       |
| actavis/Phönix             | Abitima <sup>®</sup> clinic face cream | 164225       | 1       |
| Actavis/Phönix             | Abitima <sup>®</sup> clinic face cream | 159274       | 2       |
| Actavis/Phönix             | Abitima <sup>®</sup> clinic face cream | 164225       | 1       |
| Caelo                      | Abitima <sup>®</sup> clinic face cream | 146735       | 1       |
| Caelo                      | Abitima <sup>®</sup> clinic face cream | 149666       | 2       |
| Caelo                      | Abitima <sup>®</sup> clinic face cream | 161468       | 2       |
| Caelo                      | Abitima <sup>®</sup> clinic face cream | 170180       | 1       |
| Fagron                     | Abitima <sup>®</sup> clinic face cream | 150204       | 1       |

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| Supplier                   | Substance                              | Batch       | Spectra |
|----------------------------|----------------------------------------|-------------|---------|
| Noweda                     | Abitima <sup>®</sup> clinic face cream | 146735      | 1       |
| Persano/Gehe               | Abitima <sup>®</sup> clinic face cream | 57792       | 1       |
| Phoenix/actavis            | Abitima <sup>®</sup> clinic face cream | 148460      | 1       |
| Puren                      | Abitima <sup>®</sup> clinic face cream | 169356      | 1       |
| Puren / Gehe               | Abitima <sup>®</sup> clinic face cream | 174292      | 1       |
| Puren Pharma               | Abitima <sup>®</sup> clinic face cream | 169357      | 1       |
| Puren/AHCA                 | Abitima <sup>®</sup> clinic face cream | 164225      | 1       |
| allergika pharma gmbH /... | Allergika <sup>®</sup> Base cream      | 8/072024    | 1       |
| Allergika Pharma/Sanacorp  | Allergika <sup>®</sup> Base cream      | 2012023     | 1       |
| Allergika/Phönix           | Allergika <sup>®</sup> Base cream      | 4/032023    | 1       |
| Henry Lamotte / 2          | Allergika <sup>®</sup> Base cream      | 14/102023   | 1       |
| Kehr 22.09.2020            | Allergika <sup>®</sup> Base cream      | 2/2025      | 1       |
| Aenova / Noweda            | Asche Basis <sup>®</sup> cream         | 62343A      | 1       |
| AHD/Chiesi                 | Asche Basis <sup>®</sup> cream         | 92436A      | 1       |
| All.Heal./Chiesi           | Asche Basis <sup>®</sup> cream         | 24218A      | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> cream         | 33240A      | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> cream         | 33237A      | 1       |
| Anzag                      | Asche Basis <sup>®</sup> cream         | 23204A      | 1       |
| Anzag/ Chiesi              | Asche Basis <sup>®</sup> cream         | 42269A      | 1       |
| Anzag/ Chiesi GmbH         | Asche Basis <sup>®</sup> cream         | 42272A      | 1       |
| Anzag/ Chiesi GmbH         | Asche Basis <sup>®</sup> cream         | 42273A      | 1       |
| Asche Chiesi/Alliance      | Asche Basis <sup>®</sup> cream         | 71374A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 41265B      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 52323a      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 53331A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 61341A      | 2       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 64359A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 71372A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 74398A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 83411A      | 3       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 82409A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 61340A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 91426A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 61337A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 31226A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 64364A      | 2       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 20170829Ma4 | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 52322A      | 3       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 53330A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 61335A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 73386A      | 2       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 31227A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 64363A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 53329A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 61338A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 71367A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 74391A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 81402A      | 3       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 83413A      | 1       |
| Caelo                      | Asche Basis <sup>®</sup> cream         | 72380A      | 2       |
| Chiese                     | Asche Basis <sup>®</sup> cream         | 24221A      | 1       |
| Chiese                     | Asche Basis <sup>®</sup> cream         | 41259A      | 1       |
| Chiese                     | Asche Basis <sup>®</sup> cream         | 1449A       | 1       |
| Chiese / Gehe              | Asche Basis <sup>®</sup> cream         | 74392A      | 1       |
| Chiese/Gehe                | Asche Basis <sup>®</sup> cream         | 72385A      | 1       |
| Chiese/Phönix              | Asche Basis <sup>®</sup> cream         | 82408A      | 1       |
| chiesi                     | Asche Basis <sup>®</sup> cream         | 71374A      | 1       |
| chiesi                     | Asche Basis <sup>®</sup> cream         | 82407A      | 1       |
| chiesi                     | Asche Basis <sup>®</sup> cream         | 83413A      | 1       |
| chiesi                     | Asche Basis <sup>®</sup> cream         | 84422A      | 1       |

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| Supplier | Substance                      | Batch              | Spectra |
|----------|--------------------------------|--------------------|---------|
| chiesi   | Asche Basis <sup>®</sup> cream | 84423A             | 1       |
| chiesi   | Asche Basis <sup>®</sup> cream | 94448A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 23204A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 24214A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 24219A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 23206A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 31227A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 14178A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 32233A             | 4       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 31232A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 32235A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 32236A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 24217A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 33237A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 33240A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 33243A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 34249A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 34251A             | 3       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 34250A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 34248A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 41258A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 33239A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 41261A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 41260A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 42270A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 30102014A          | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 42272A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 42271A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 43280A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 42275A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 43278A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 43262A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 43287A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 43279A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 44290A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 51300A             | 4       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 51294A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 51296A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 51305A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 52307A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 52308A             | 3       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 52309A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 52322A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 53331A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 53326A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 52310A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 53330A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 54332A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 61338A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 53329A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 62343A             | 3       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 63347A             | 5       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 63354A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 63350A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 63355A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 64357A             | 3       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 64360A             | 2       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 64362A-20170704Ma4 | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 64359A             | 1       |
| Chiesi   | Asche Basis <sup>®</sup> cream | 64364A             | 1       |

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| Supplier                     | Substance                      | Batch              | Spectra |
|------------------------------|--------------------------------|--------------------|---------|
| Chiesi                       | Asche Basis <sup>®</sup> cream | 71374A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 71370A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 72380A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 72378A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 72375A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 72383A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 73387A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 74390A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 74393A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 74392A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 74398A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 81400A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 1 (81404A)         | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 81399A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 81401A             | 5       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 81403A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 81402A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 83411A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 83412A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 84417A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 84424A             | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 84422A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 83415A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 84419A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 83413A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 91425A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 91429A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 91431A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 92434A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 92436A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 92432A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 94448AI            | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 94448AII           | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 92437A             | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 2456A              | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> cream | 4003A              | 1       |
| CHiesi                       | Asche Basis <sup>®</sup> cream | 41264A             | 1       |
| chiesi-                      | Asche Basis <sup>®</sup> cream | 71372A20171127Ma13 | 1       |
| chiesi-                      | Asche Basis <sup>®</sup> cream | 72376A-20180830Ma8 | 1       |
| Chiesi / Alliance Healt. ... | Asche Basis <sup>®</sup> cream | 82410A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 33244A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 34252A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 41265A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 43281A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 42273A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 51292A             | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> cream | 52314A             | 1       |
| chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 23213A             | 1       |
| chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 31222A             | 1       |
| chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 31225A             | 1       |
| chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 34250A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 33238A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 33246A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 51300A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 54332A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 71374A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 72380A             | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 73386A             | 2       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 74393A             | 2       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> cream | 81399A             | 2       |

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| Supplier                   | Substance                      | Batch  | Spectra |
|----------------------------|--------------------------------|--------|---------|
| Chiesi / Noweda            | Asche Basis <sup>®</sup> cream | 84417A | 1       |
| Chiesi / Noweda            | Asche Basis <sup>®</sup> cream | 91426A | 1       |
| Chiesi / Noweda            | Asche Basis <sup>®</sup> cream | 92435A | 1       |
| Chiesi / Noweda            | Asche Basis <sup>®</sup> cream | 92442A | 1       |
| CHIESI / Noweda            | Asche Basis <sup>®</sup> cream | 51299A | 3       |
| Chiesi / Phoenix           | Asche Basis <sup>®</sup> cream | 51300A | 1       |
| Chiesi / Phoenix           | Asche Basis <sup>®</sup> cream | 52323A | 2       |
| Chiesi / Phoenix WE: 06... | Asche Basis <sup>®</sup> cream | 53325A | 1       |
| chiesi / Jenne             | Asche Basis <sup>®</sup> cream | 31227a | 1       |
| Chiesi /jenne              | Asche Basis <sup>®</sup> cream | 84418A | 2       |
| Chiesi /jenne              | Asche Basis <sup>®</sup> cream | 84422A | 4       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 91427A | 1       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 91431A | 2       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 92433A | 1       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 92432A | 1       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 93445A | 2       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 93447A | 1       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 1449A  | 2       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 1451A  | 2       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 2459A  | 1       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 2458A  | 5       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 4002A  | 2       |
| Chiesi /Jenne              | Asche Basis <sup>®</sup> cream | 4003A  | 2       |
| Chiesi /Phönix             | Asche Basis <sup>®</sup> cream | 91430A | 1       |
| chiesi gmbh                | Asche Basis <sup>®</sup> cream | 72380A | 1       |
| chiesi gmbh                | Asche Basis <sup>®</sup> cream | 82410A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 24214A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 52319A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 61335A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 64363A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 64365A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 72379A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 74394A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 72382A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 81402A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 82407A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 84422A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 91426A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 84419A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 93447A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 92439A | 1       |
| Chiesi GmbH                | Asche Basis <sup>®</sup> cream | 92437A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 22196A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 31222A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 31230A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 31229A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 31231A | 2       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 33244A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 34249A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 41260A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 41261A | 1       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 42268A | 2       |
| Chiesi GmbH / Anzag        | Asche Basis <sup>®</sup> cream | 74394A | 1       |
| Chiesi GmbH / Sanacorp     | Asche Basis <sup>®</sup> cream | 34247A | 1       |
| Chiesi GmbH/ Alliance H... | Asche Basis <sup>®</sup> cream | 83415A | 1       |
| Chiesi GmbH/ Noweda        | Asche Basis <sup>®</sup> cream | 74396A | 1       |
| Chiesi GmbH/ Noweda        | Asche Basis <sup>®</sup> cream | 84418A | 1       |
| Chiesi GmbH/ Noweda        | Asche Basis <sup>®</sup> cream | 91425A | 1       |
| Chiesi GmbH/ Noweda        | Asche Basis <sup>®</sup> cream | 84420A | 1       |
| Chiesi GmbH/AHD            | Asche Basis <sup>®</sup> cream | 1453A  | 1       |

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| Supplier                  | Substance                      | Batch            | Spectra |
|---------------------------|--------------------------------|------------------|---------|
| Chiesi GmbH/Phoenix       | Asche Basis <sup>®</sup> cream | 93443A           | 1       |
| Chiesi GmbH/Phoenix       | Asche Basis <sup>®</sup> cream | 2456A            | 1       |
| Chiesi GmbH/Phoenix       | Asche Basis <sup>®</sup> cream | 4004A            | 1       |
| Sino Phyto                | Asche Basis <sup>®</sup> cream | 74394A           | 1       |
| Sino Phyto                | Asche Basis <sup>®</sup> cream | 92436A           | 2       |
| Chiesi Sanacorp           | Asche Basis <sup>®</sup> cream | 81404A           | 1       |
| Chiesi/                   | Asche Basis <sup>®</sup> cream | 41266A           | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 64358A           | 3       |
| Chiesi/ Fiebig            | Asche Basis <sup>®</sup> cream | 63356A           | 1       |
| Chiesi/ Fiebig            | Asche Basis <sup>®</sup> cream | 64363A           | 2       |
| Chiesi/ Fiebig            | Asche Basis <sup>®</sup> cream | 72376A           | 2       |
| Chiesi/ Fiebig            | Asche Basis <sup>®</sup> cream | 74392A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 52323A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 82410A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 83411A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 73386A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 84424A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 92435A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 92436A           | 1       |
| Chiesi/ Gehe              | Asche Basis <sup>®</sup> cream | 1453A            | 1       |
| Chiesi/ Now               | Asche Basis <sup>®</sup> cream | 33240A           | 1       |
| Chiesi/ Now               | Asche Basis <sup>®</sup> cream | 41259A           | 1       |
| Chiesi/ Now               | Asche Basis <sup>®</sup> cream | 42273A           | 1       |
| Chiesi/ Now               | Asche Basis <sup>®</sup> cream | 43282A           | 1       |
| Chiesi/ Now               | Asche Basis <sup>®</sup> cream | 43283A           | 2       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 51294a           | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 52307A           | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170420AB/63353A  | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170601ABC/64357A | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170628ABC/64362A | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170706ABC/64361A | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170816AB/64364A  | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 170927AB/71370A  | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 171025AB/71371A  | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 71371A           | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 171215ABC/72376A | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 171228ABC/72376A | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 180219AB/72379A  | 1       |
| Chiesi/ Noweda            | Asche Basis <sup>®</sup> cream | 73389A           | 1       |
| Chiesi/ phoenix           | Asche Basis <sup>®</sup> cream | 33239A           | 1       |
| Chiesi/ Phoenix/ 13.11... | Asche Basis <sup>®</sup> cream | 91427A           | 1       |
| Chiesi/ Phönix            | Asche Basis <sup>®</sup> cream | 84421A           | 1       |
| Chiesi/ Sanacorp          | Asche Basis <sup>®</sup> cream | 92434A           | 1       |
| Chiesi/ Sanacorp          | Asche Basis <sup>®</sup> cream | 93443A           | 1       |
| Chiesi//Phönix            | Asche Basis <sup>®</sup> cream | 63354A           | 1       |
| Chiesi/4                  | Asche Basis <sup>®</sup> cream | 83412A           | 1       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 71368A           | 1       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 72385A           | 1       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 73386A           | 2       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 73388A           | 4       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 74394A           | 1       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 82405A           | 2       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 84421A           | 1       |
| Chiesi/AEP                | Asche Basis <sup>®</sup> cream | 91428A           | 2       |
| Chiesi/AHCA               | Asche Basis <sup>®</sup> cream | 74396A           | 2       |
| Chiesi/AHCA               | Asche Basis <sup>®</sup> cream | 82409A           | 2       |
| Chiesi/AHD                | Asche Basis <sup>®</sup> cream | 31222A           | 1       |
| Chiesi/AHD                | Asche Basis <sup>®</sup> cream | 31223A           | 1       |
| Chiesi/AHD                | Asche Basis <sup>®</sup> cream | 31224A           | 1       |
| Chiesi/AHD                | Asche Basis <sup>®</sup> cream | 31228A           | 2       |

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| Supplier                   | Substance                      | Batch   | Spectra |
|----------------------------|--------------------------------|---------|---------|
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 32234A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 32235A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 33242A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 33238A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 34247A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 81404A  | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 2456A   | 1       |
| Chiesi/AHD                 | Asche Basis <sup>®</sup> cream | 4002A   | 1       |
| Chiesi/Alliance            | Asche Basis <sup>®</sup> cream | 61338A  | 1       |
| Chiesi/Alliance Healthc... | Asche Basis <sup>®</sup> cream | 44290A  | 4       |
| Chiesi/Alliance Healthc... | Asche Basis <sup>®</sup> cream | 52306A  | 3       |
| Chiesi/Alliance Healthc... | Asche Basis <sup>®</sup> cream | 52323A  | 4       |
| Chiesi/Alliance Healthc... | Asche Basis <sup>®</sup> cream | 53329A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 24221A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 43282A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 51295A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 53329A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 53327A  | 1       |
| Chiesi/Anzag               | Asche Basis <sup>®</sup> cream | 92437A  | 1       |
| Chiesi/Ebert               | Asche Basis <sup>®</sup> cream | 31224A  | 1       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 733864A | 1       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 74396A  | 1       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 81400A  | 2       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 81399A  | 1       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 92436A  | 1       |
| Chiesi/Fiebig              | Asche Basis <sup>®</sup> cream | 92434A  | 1       |
| chiesi/gehe                | Asche Basis <sup>®</sup> cream | 31228A  | 1       |
| chiesi/gehe                | Asche Basis <sup>®</sup> cream | 32236A  | 1       |
| chiesi/gehe                | Asche Basis <sup>®</sup> cream | 33246A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 24221A  | 4       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 24218A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 31224A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 32233A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 34248A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 34253A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 41262A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 41260A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 42271A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 43278A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 51300A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 51301A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 52307A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 63350A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 71371A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 72379A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 72381A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 73388A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 74390A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 81400A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 81401A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 81402A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 82408A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 82409A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 83413A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 84420A  | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 941426A | 1       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 91426A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 91429A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 91430A  | 2       |
| Chiesi/Gehe                | Asche Basis <sup>®</sup> cream | 91425A  | 1       |

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| Supplier       | Substance                      | Batch            | Spectra |
|----------------|--------------------------------|------------------|---------|
| Chiesi/Gehe    | Asche Basis <sup>®</sup> cream | 92434A           | 1       |
| Chiesi/Gehe    | Asche Basis <sup>®</sup> cream | 92439A           | 1       |
| Chiesi/Insel   | Asche Basis <sup>®</sup> cream | 74391A           | 1       |
| Chiesi/Jenne   | Asche Basis <sup>®</sup> cream | 83413A           | 1       |
| Chiesi/Jenne   | Asche Basis <sup>®</sup> cream | 84421A           | 2       |
| Chiesi/Jenne   | Asche Basis <sup>®</sup> cream | 91429A           | 3       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 81402A           | 2       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 82409A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 83416A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 83414A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 84421A           | 2       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 84423A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 84422A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 91427A           | 1       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 92432A           | 2       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 92439A           | 2       |
| Chiesi/Kehr    | Asche Basis <sup>®</sup> cream | 2460A            | 2       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 64363A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 72379A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 72384A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 72383A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 74396A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 81403A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 82407A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 82409A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 91427A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 92435A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 91430A           | 2       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 91431A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 93444A           | 1       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 1452A            | 2       |
| Chiesi/Krieger | Asche Basis <sup>®</sup> cream | 1449A            | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 31224A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 31229A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 31232A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 33237A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 34247A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 41258A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 42275A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 43280A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 44288A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 52306A           | 2       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 52318A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 53329A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 52318a           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 6234A            | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 63347A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 170421AB/63353A  | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 171211AB/72376A  | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 180112ABC/72378A | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 180322AB/72382A  | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 74394A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 84424A           | 2       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 84419A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 92433A           | 1       |
| Chiesi/Noweda  | Asche Basis <sup>®</sup> cream | 92440A           | 1       |
| Chiesi/Phoenix | Asche Basis <sup>®</sup> cream | 24215A           | 1       |
| Chiesi/Phoenix | Asche Basis <sup>®</sup> cream | 31227A           | 2       |
| Chiesi/Phoenix | Asche Basis <sup>®</sup> cream | 31225A           | 1       |
| Chiesi/Phoenix | Asche Basis <sup>®</sup> cream | 31229A           | 1       |

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| Supplier                   | Substance                      | Batch  | Spectra |
|----------------------------|--------------------------------|--------|---------|
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 32233A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 43278A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 71368A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 72377A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 72383A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 74394A | 1       |
| Chiesi/Phoenix             | Asche Basis <sup>®</sup> cream | 84418A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 53329A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 61334A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 64358A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 71367A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 72375A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 72385A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 73388A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 74394A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 81404A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 81400A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 82405A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 81402A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 81401A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 82407A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 84417A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 83412A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 83416A | 4       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 84418A | 4       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 84420A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 84421A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 84419A | 3       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 91426A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 91429A | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92435A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 91427A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 91425A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92434A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92432A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92441A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92437A | 3       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 92438A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 93443A | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 1451A  | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> cream | 2459A  | 1       |
| Chiesi/Phönix WE:19.05...  | Asche Basis <sup>®</sup> cream | 64357A | 1       |
| Chiesi/Phönix WE:20.06...  | Asche Basis <sup>®</sup> cream | 64362A | 2       |
| Chiesi/Phönix WE:27.05...  | Asche Basis <sup>®</sup> cream | 52309A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 31227A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 74394A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 82408A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 83412A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 83413A | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> cream | 84418A | 1       |
| Chiesi/Sanacorp 311.15     | Asche Basis <sup>®</sup> cream | 51305A | 3       |
| Chiesi/Sanacorp WE:06.0... | Asche Basis <sup>®</sup> cream | 52317A | 1       |
| Spangropharm               | Asche Basis <sup>®</sup> cream | 82093A | 1       |
| Chiesi/V.d.L.              | Asche Basis <sup>®</sup> cream | 34250A | 1       |
| Chiesi/VDL                 | Asche Basis <sup>®</sup> cream | 92436A | 1       |
| Chiesi/VDL                 | Asche Basis <sup>®</sup> cream | 1455A  | 1       |
| Chiesie                    | Asche Basis <sup>®</sup> cream | 84417A | 1       |
| Chiesie                    | Asche Basis <sup>®</sup> cream | 92436A | 1       |
| Chiesie                    | Asche Basis <sup>®</sup> cream | 92439A | 1       |
| Chiesie GmbH/Phönix        | Asche Basis <sup>®</sup> cream | 83415A | 1       |

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| Supplier               | Substance                      | Batch                | Spectra |
|------------------------|--------------------------------|----------------------|---------|
| Chiesie GmbH/Phönix    | Asche Basis <sup>®</sup> cream | 91425A               | 2       |
| Chiesie GmbH/Phönix    | Asche Basis <sup>®</sup> cream | 92432A               | 1       |
| Chiesie GmbH/Phönix    | Asche Basis <sup>®</sup> cream | 4002A                | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> cream | 71372A               | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> cream | 81401A-A20190115Ma11 | 1       |
| Chiesi-Fa.Gehe 19.6.18 | Asche Basis <sup>®</sup> cream | 74391A-20180830Ma7   | 1       |
| Chiesi-Phönix          | Asche Basis <sup>®</sup> cream | 91430A               | 2       |
| Chiesi-Phönix          | Asche Basis <sup>®</sup> cream | 91425A               | 1       |
| Chisei                 | Asche Basis <sup>®</sup> cream | 72382A               | 1       |
| Chisesi                | Asche Basis <sup>®</sup> cream | 52310A               | 1       |
| Chisesi/Noweda         | Asche Basis <sup>®</sup> cream | 53331A               | 1       |
| Chisesi/Noweda         | Asche Basis <sup>®</sup> cream | 61338A               | 1       |
| Chisesi/Noweda         | Asche Basis <sup>®</sup> cream | 71367A               | 1       |
| Chisi                  | Asche Basis <sup>®</sup> cream | 23203A               | 1       |
| Chisie/ Jenne          | Asche Basis <sup>®</sup> cream | 91431A               | 1       |
| Chisie/VDL             | Asche Basis <sup>®</sup> cream | 84417A               | 2       |
| Euro OTC               | Asche Basis <sup>®</sup> cream | 3229A                | 1       |
| Euro OTC               | Asche Basis <sup>®</sup> cream | 61337A               | 2       |
| Fa.Gehe                | Asche Basis <sup>®</sup> cream | 20160727Ma4          | 1       |
| Fagron                 | Asche Basis <sup>®</sup> cream | 63353A               | 1       |
| Fiebig                 | Asche Basis <sup>®</sup> cream | 83413A               | 3       |
| Fiebig                 | Asche Basis <sup>®</sup> cream | 84420A               | 1       |
| Fiebig                 | Asche Basis <sup>®</sup> cream | 84421A               | 1       |
| Fiebig                 | Asche Basis <sup>®</sup> cream | 91428A               | 2       |
| Fiebig/Chiesi GmbH     | Asche Basis <sup>®</sup> cream | 73388A               | 1       |
| Fiebig/Chiesi GmbH     | Asche Basis <sup>®</sup> cream | 81404A               | 1       |
| Galaderma/Krieger      | Asche Basis <sup>®</sup> cream | 17370A               | 1       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 32236A               | 1       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 33244A               | 1       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 52321A               | 1       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 61334A               | 1       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 64358A               | 2       |
| Gehe                   | Asche Basis <sup>®</sup> cream | 64360A               | 1       |
| GEHE                   | Asche Basis <sup>®</sup> cream | 73387A               | 2       |
| GEHE                   | Asche Basis <sup>®</sup> cream | 81399A               | 1       |
| GEHE                   | Asche Basis <sup>®</sup> cream | 82410A               | 1       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 52318A               | 2       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 32233A               | 1       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 51296A               | 1       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 84418A               | 2       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 1452A                | 1       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> cream | 92440A               | 1       |
| Gehe-Chiesi            | Asche Basis <sup>®</sup> cream | 52308A               | 1       |
| Gepepharm/VDL          | Asche Basis <sup>®</sup> cream | 81399A               | 1       |
| Hedinger               | Asche Basis <sup>®</sup> cream | 74398A               | 1       |
| Hedinger/Noweda        | Asche Basis <sup>®</sup> cream | 82405A               | 1       |
| Ichthyol/Sanacorp      | Asche Basis <sup>®</sup> cream | 24221A               | 1       |
| Insel                  | Asche Basis <sup>®</sup> cream | 72378A               | 1       |
| Kremer                 | Asche Basis <sup>®</sup> cream | 71367A               | 3       |
| krieger                | Asche Basis <sup>®</sup> cream | 92436A               | 1       |
| Lamotte / Gehe         | Asche Basis <sup>®</sup> cream | 34247A               | 1       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 81399A               | 1       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 82410A               | 1       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 83411A               | 2       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 84417A               | 4       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 84424A               | 3       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 92435A               | 2       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 92436A               | 4       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 92442A               | 2       |
| Noweda                 | Asche Basis <sup>®</sup> cream | 1453A                | 2       |

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| Supplier                   | Substance                       | Batch               | Spectra |
|----------------------------|---------------------------------|---------------------|---------|
| Noweda                     | Asche Basis <sup>®</sup> cream  | 1455A               | 2       |
| Noweda                     | Asche Basis <sup>®</sup> cream  | 3461A               | 2       |
| Noweda/Apomix              | Asche Basis <sup>®</sup> cream  | 92433A              | 1       |
| noweda/chiesi              | Asche Basis <sup>®</sup> cream  | 52306A              | 1       |
| Noweda/Chiesi              | Asche Basis <sup>®</sup> cream  | 73386A              | 1       |
| Noweda/Chiesi              | Asche Basis <sup>®</sup> cream  | 82410A              | 1       |
| Noweda/Chiesi              | Asche Basis <sup>®</sup> cream  | 84424A              | 1       |
| Noweda/Chiesi              | Asche Basis <sup>®</sup> cream  | 94448A              | 1       |
| Phoenix                    | Asche Basis <sup>®</sup> cream  | 53331A              | 1       |
| Phoenix                    | Asche Basis <sup>®</sup> cream  | 54332A              | 1       |
| Phoenix WE 13.04.17 -7,... | Asche Basis <sup>®</sup> cream  | 63353A              | 2       |
| Phoenix WE: 08.11.17 10... | Asche Basis <sup>®</sup> cream  | 71372A              | 1       |
| Phoenix WE: 09.10.17 50... | Asche Basis <sup>®</sup> cream  | 71368A              | 1       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> cream  | 33246A              | 1       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> cream  | 61333A              | 1       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> cream  | 64358A              | 1       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> cream  | 73387A              | 1       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> cream  | 81399A              | 1       |
| Phönix                     | Asche Basis <sup>®</sup> cream  | 322344              | 1       |
| Phönix                     | Asche Basis <sup>®</sup> cream  | 81404A              | 1       |
| PHÖNIX                     | Asche Basis <sup>®</sup> cream  | 62343A              | 1       |
| PHÖNIX                     | Asche Basis <sup>®</sup> cream  | 73386A              | 1       |
| Phönix /Chiesi             | Asche Basis <sup>®</sup> cream  | 81402A              | 1       |
| phönix WE: 28.08.17 EK...  | Asche Basis <sup>®</sup> cream  | 64365A              | 2       |
| Phönix/ Chiesi             | Asche Basis <sup>®</sup> cream  | 91425A              | 1       |
| PhönixWE:3.02.2017 EK...   | Asche Basis <sup>®</sup> cream  | 63350A              | 1       |
| Sanacoro W.E:01.03.18 ...  | Asche Basis <sup>®</sup> cream  | 72378A              | 1       |
| Sanacoro W.E:01.03.18 ...  | Asche Basis <sup>®</sup> cream  | 72379A              | 2       |
| Sanacorp                   | Asche Basis <sup>®</sup> cream  | 53327A              | 1       |
| SANACORP                   | Asche Basis <sup>®</sup> cream  | 84417A              | 2       |
| SANACORP                   | Asche Basis <sup>®</sup> cream  | 92435A              | 1       |
| Sanacorp /100ml            | Asche Basis <sup>®</sup> cream  | 72382A              | 2       |
| Sanacorp EK:8,07 EUR...    | Asche Basis <sup>®</sup> cream  | 64363A              | 1       |
| Sanacorp EK:8,07 EUR...    | Asche Basis <sup>®</sup> cream  | 64364A              | 1       |
| Sanacorp / Wolff           | Asche Basis <sup>®</sup> cream  | 82A05A              | 1       |
| Sanacorp /Chiesi           | Asche Basis <sup>®</sup> cream  | 84418A              | 1       |
| Sanacorp W.E: 02.02.18 ... | Asche Basis <sup>®</sup> cream  | 72377A              | 1       |
| Sanacorp WE 20.02.17 -7... | Asche Basis <sup>®</sup> cream  | 63351A              | 3       |
| THC/ Phönix Pharma Eink... | Asche Basis <sup>®</sup> cream  | 129880              | 1       |
| WE Sanacorp                | Asche Basis <sup>®</sup> cream  | 61341A              | 1       |
| WE: Phoenix 07.10.2016 ... | Asche Basis <sup>®</sup> cream  | 61340A              | 1       |
| WE: Phoenix 23.09.2016 ... | Asche Basis <sup>®</sup> cream  | 61339A              | 1       |
| WE:Phönix28.07.2016 E...   | Asche Basis <sup>®</sup> cream  | 61336A              | 1       |
| Wolff/ Sanacorp            | Asche Basis <sup>®</sup> cream  | 810201              | 1       |
| Wolff/Gehe                 | Asche Basis <sup>®</sup> cream  | 71366A              | 1       |
| Wolff/Gehe                 | Asche Basis <sup>®</sup> cream  | 64365A-20171106Ma10 | 1       |
| Aenov Groupe               | Asche Basis <sup>®</sup> lotion | 40000200790         | 1       |
| Aenova                     | Asche Basis <sup>®</sup> lotion | 93102A              | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 73087A              | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 63981A              | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 73089A              | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 82094A              | 2       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 91098A              | 3       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 91099A              | 1       |
| Alliance Healthcare        | Asche Basis <sup>®</sup> lotion | 92100A              | 3       |
| Asche Chiesi/Alliance      | Asche Basis <sup>®</sup> lotion | 73087A              | 1       |
| Caelo                      | Asche Basis <sup>®</sup> lotion | 33055A              | 3       |
| Caelo                      | Asche Basis <sup>®</sup> lotion | 32054A              | 1       |
| Caelo                      | Asche Basis <sup>®</sup> lotion | 53075A              | 1       |
| Caelo                      | Asche Basis <sup>®</sup> lotion | 53073A              | 1       |

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| Supplier                    | Substance                       | Batch   | Spectra |
|-----------------------------|---------------------------------|---------|---------|
| Caelo                       | Asche Basis <sup>®</sup> lotion | 53072A  | 1       |
| Caelo                       | Asche Basis <sup>®</sup> lotion | 73089A  | 1       |
| Chiese                      | Asche Basis <sup>®</sup> lotion | 41060A  | 1       |
| chiesi                      | Asche Basis <sup>®</sup> lotion | 84095A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 333056A | 2       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 32054A  | 2       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 41059A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 43066A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 53072A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 53075A  | 2       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 53073A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 61077A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 46082A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 73087A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 75085A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 73088A  | 3       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 73088a  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 82094A  | 1       |
| Chiesi                      | Asche Basis <sup>®</sup> lotion | 92101A  | 1       |
| Chiesi / Noweda / 07.08...  | Asche Basis <sup>®</sup> lotion | 84095A  | 1       |
| Chiesi / Noweda / 09.04...  | Asche Basis <sup>®</sup> lotion | 82093A  | 1       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 53071A  | 3       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 53072A  | 2       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 61076A  | 2       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 53074A  | 1       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 63078A  | 2       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 63079A  | 2       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 63980A  | 1       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 73087A  | 1       |
| Chiesi GmbH                 | Asche Basis <sup>®</sup> lotion | 92100A  | 1       |
| Chiesi GmbH / Phönix        | Asche Basis <sup>®</sup> lotion | 51067A  | 1       |
| Chiesi GmbH/Gehe            | Asche Basis <sup>®</sup> lotion | 53072A  | 1       |
| Chiesi/ Noweda              | Asche Basis <sup>®</sup> lotion | 64082A  | 1       |
| Chiesi/ Fiebig              | Asche Basis <sup>®</sup> lotion | 63980A  | 1       |
| Chiesi/ Phoenix/ 04.03...   | Asche Basis <sup>®</sup> lotion | 93103A  | 1       |
| Chiesi/ Phoenix/ 23.10...   | Asche Basis <sup>®</sup> lotion | 92100A  | 1       |
| Chiesi/ Phoenix/ 30.11...   | Asche Basis <sup>®</sup> lotion | 1108A   | 1       |
| Chiesi/ Phoenix/ 11.08.2... | Asche Basis <sup>®</sup> lotion | 94104A  | 1       |
| Chiesi/ Phönix              | Asche Basis <sup>®</sup> lotion | 43066A  | 1       |
| Chiesi/AHD                  | Asche Basis <sup>®</sup> lotion | 24049A  | 1       |
| Chiesi/AHD/ 21.12.2020/...  | Asche Basis <sup>®</sup> lotion | 1107A   | 1       |
| Chiesi/Alliance             | Asche Basis <sup>®</sup> lotion | 63981A  | 1       |
| Chiesi/Anzag                | Asche Basis <sup>®</sup> lotion | 41059A  | 2       |
| Chiesi/Anzag                | Asche Basis <sup>®</sup> lotion | 53075A  | 2       |
| Chiesi/E+J                  | Asche Basis <sup>®</sup> lotion | 64082A  | 1       |
| Chiesi/Fa.Gehe              | Asche Basis <sup>®</sup> lotion | 53075A  | 1       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 53073A  | 2       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 53074A  | 1       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 63980A  | 1       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 73086A  | 1       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 82092A  | 2       |
| Chiesi/Fiebig               | Asche Basis <sup>®</sup> lotion | 92100A  | 1       |
| chiesi/gehe                 | Asche Basis <sup>®</sup> lotion | 33056A  | 2       |
| chiesi/gehe                 | Asche Basis <sup>®</sup> lotion | 34058A  | 1       |
| Chiesi/Gehe                 | Asche Basis <sup>®</sup> lotion | 23047A  | 1       |
| Chiesi/Gehe                 | Asche Basis <sup>®</sup> lotion | 64082A  | 1       |
| Chiesi/Krieger              | Asche Basis <sup>®</sup> lotion | 64082A  | 1       |
| Chiesi/Krieger              | Asche Basis <sup>®</sup> lotion | 82092A  | 3       |
| Chiesi/Noweda               | Asche Basis <sup>®</sup> lotion | 61077A  | 1       |
| Chiesi/Noweda               | Asche Basis <sup>®</sup> lotion | 64082A  | 1       |

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| Supplier               | Substance                       | Batch               | Spectra |
|------------------------|---------------------------------|---------------------|---------|
| Chiesi/Noweda          | Asche Basis <sup>®</sup> lotion | 71083A              | 1       |
| Chiesi/Noweda          | Asche Basis <sup>®</sup> lotion | 73089A              | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> lotion | 52070A              | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> lotion | 53071A              | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> lotion | 64082A              | 1       |
| Chiesi/Phonix          | Asche Basis <sup>®</sup> lotion | 91097A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 53071A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 53073A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 63078A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 63981A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 73086A              | 2       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 84095A              | 2       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 82092A              | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> lotion | 92100A              | 1       |
| Chiesi/Sanacorp        | Asche Basis <sup>®</sup> lotion | 91097A              | 1       |
| Chiesie/Anzag          | Asche Basis <sup>®</sup> lotion | 32054A              | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> lotion | 64082A-20180112Ma3  | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> lotion | 73087A-20180206Ma9  | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> lotion | 73086A-20180206Ma8  | 1       |
| Chiesi-Fa.Gehe         | Asche Basis <sup>®</sup> lotion | 82093A-A20181115Ma1 | 1       |
| Chiesi-Fa.Gehe 19.7.18 | Asche Basis <sup>®</sup> lotion | 74090A-20180830Ma10 | 1       |
| Ebert & Jacobi         | Asche Basis <sup>®</sup> lotion | 73088A              | 1       |
| Fa.Gehe                | Asche Basis <sup>®</sup> lotion | 20160727Ma5         | 1       |
| Fiebig                 | Asche Basis <sup>®</sup> lotion | 91097A              | 1       |
| Caelo                  | Asche Basis <sup>®</sup> lotion | 63078A              | 1       |
| Fiebig/Chiesi          | Asche Basis <sup>®</sup> lotion | 71083A              | 1       |
| Fiebig/Chiesi          | Asche Basis <sup>®</sup> lotion | 71084A              | 3       |
| Fiebig/Chiesi          | Asche Basis <sup>®</sup> lotion | 73087A              | 2       |
| Fiebig/Chiesi          | Asche Basis <sup>®</sup> lotion | 84095A              | 1       |
| Gehe                   | Asche Basis <sup>®</sup> lotion | 82082A              | 1       |
| Gehe Chiesi            | Asche Basis <sup>®</sup> lotion | 53075A-20160615Ma5  | 1       |
| Caelo                  | Asche Basis <sup>®</sup> lotion | 64082A              | 3       |
| gehe/Chiesi            | Asche Basis <sup>®</sup> lotion | 43066A              | 1       |
| Gehe/Chiesi            | Asche Basis <sup>®</sup> lotion | 93103A              | 1       |
| Gehe20.10.15           | Asche Basis <sup>®</sup> lotion | 52070A              | 1       |
| Noweda                 | Asche Basis <sup>®</sup> lotion | 63980A              | 1       |
| Noweda                 | Asche Basis <sup>®</sup> lotion | 93103A              | 4       |
| Bombastus              | Asche Basis <sup>®</sup> lotion | 74091A              | 1       |
| Caelo                  | Asche Basis <sup>®</sup> lotion | 64082a              | 1       |
| Phoenix                | Asche Basis <sup>®</sup> lotion | 52069A              | 1       |
| PHÖNIX                 | Asche Basis <sup>®</sup> 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              | 160201-6027         | 1       |
| Taoasis                | Base cream Taoasis              | 161124-6322         | 1       |
| Taoasis                | Base cream Taoasis              | 170110-6322         | 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       |

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| Supplier                     | Substance                           | Batch       | Spectra |
|------------------------------|-------------------------------------|-------------|---------|
| 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       |
| dermasence                   | Dermatest base ointment             | 260820      | 2       |
| 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/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 <sup>®</sup> base cream    | 8F075A      | 1       |
| Phönix                       | Dermatop <sup>®</sup> base cream    | 7F072A      | 2       |
| Phönix                       | Dermatop <sup>®</sup> base cream    | 8F076A      | 1       |
| Sanofi                       | Dermatop <sup>®</sup> base cream    | 4F046A      | 1       |
| Sanofi                       | Dermatop <sup>®</sup> base cream    | 0F092A      | 1       |
| Sanofi                       | Dermatop <sup>®</sup> base cream    | F092A       | 1       |
| Sanofi / Gehe                | Dermatop <sup>®</sup> base cream    | 4F046A      | 1       |
| Sanofi Aventis               | Dermatop <sup>®</sup> base cream    | 4F046A      | 1       |
| Sanofi/AllianceHealthcare    | Dermatop <sup>®</sup> base cream    | F091A       | 2       |
| Sanofi/Anzag                 | Dermatop <sup>®</sup> base cream    | 5F051A      | 1       |
| Sanofi/Anzag                 | Dermatop <sup>®</sup> base cream    | 5F056A      | 1       |
| Sanofi/Gehe                  | Dermatop <sup>®</sup> base cream    | 4F050A      | 1       |
| Sanofi/Noweda                | Dermatop <sup>®</sup> base cream    | 5F056A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 4F046A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 5F051A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 7F071A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 7F073A      | 2       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 7F069A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F074A      | 2       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F078A      | 2       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F079A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F076A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F081A      | 2       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F084A      | 3       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F082B      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F083A      | 3       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 9F086A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 8F082A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 9F089A      | 1       |
| Sanofi/Phönix                | Dermatop <sup>®</sup> base cream    | 9F087A      | 1       |
| Sanofi/Sanacorp              | Dermatop <sup>®</sup> base cream    | 7F071A      | 1       |
| Sanofi-Aventis/Gehe          | Dermatop <sup>®</sup> base cream    | 5F051A      | 1       |
| Sanofi-Aventis/Phönix        | Dermatop <sup>®</sup> base cream    | 6F065A      | 1       |
| KOKO GmbH                    | DMS <sup>®</sup> base cream classic | L005A14     | 1       |
| KOKO GmbH                    | DMS <sup>®</sup> base cream classic | L003E16     | 1       |
| KOKO GmbH & Co KG            | DMS <sup>®</sup> base cream classic | L062H18     | 6       |
| KOKO GmbH & Co KG            | DMS <sup>®</sup> base cream classic | L036I18     | 2       |
| KOKO GmbH & Co KG            | DMS <sup>®</sup> base cream classic | L036I18     | 1       |
| KOKO GmbH & Co KG            | DMS <sup>®</sup> base cream classic | L036I18     | 2       |
| koko GmbH EK: EUR 38,30 /... | DMS <sup>®</sup> base cream classic | L008F17     | 1       |

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| Supplier                   | Substance                                   | Batch        | Spectra |
|----------------------------|---------------------------------------------|--------------|---------|
| Koko GmbH&Co KG            | DMS <sup>®</sup> base cream classic         | L038J16      | 1       |
| KoKo GmbH/KoKo GmbH        | DMS <sup>®</sup> base cream classic         | 11090E19     | 1       |
| Caelo                      | DMS <sup>®</sup> base cream high classic    | L010J15      | 1       |
| Caelo                      | DMS <sup>®</sup> base cream high classic    | L047117      | 4       |
| KOKO                       | DMS <sup>®</sup> base cream high classic    | L031A14      | 1       |
| Koko GmbH                  | DMS <sup>®</sup> base cream high classic    | L019H17      | 1       |
| Koko GmbH                  | DMS <sup>®</sup> base cream high classic    | L033J17      | 3       |
| Koko GmbH                  | DMS <sup>®</sup> base cream high classic    | L031D18      | 1       |
| Koko GmbH                  | DMS <sup>®</sup> base cream high classic    | L031A14      | 1       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L010E17      | 10      |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L019H17      | 5       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L008K17      | 5       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | 1028c18      | 5       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L042E18      | 5       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | 1053f18      | 3       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L050I18      | 5       |
| KOKO GmbH                  | DMS <sup>®</sup> base cream high classic    | L030L16      | 3       |
| KOKO GmbH & Co. KG         | DMS <sup>®</sup> base cream high classic    | L054B16      | 1       |
| Koko GmbH                  | DMS <sup>®</sup> base cream high classic... | L035F17      | 1       |
| KOKO GmbH & Co. KG         | DMS <sup>®</sup> base cream high classic... | L018D16      | 1       |
| Beiersdorf                 | Eucerinum O/W basis                         | 319030108WA  | 1       |
| Beiersdorf                 | Eucerinum O/W basis                         | 24830308WA   | 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                         | 84030208WA   | 1       |
| Beiersdorf / Noweda        | Eucerinum O/W basis                         | 94830108WA   | 1       |
| Beiersdorf AG              | Eucerinum O/W basis                         | 24830308WA   | 1       |
| Beiersdorf AG              | Eucerinum O/W basis                         | 2483030308WA | 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       |
| 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                         | 84030208WA   | 4       |
| Beiersdorf/Kehr            | Eucerinum O/W basis                         | 84030108WA   | 3       |
| 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       |

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| Supplier                     | Substance           | Batch       | Spectra |
|------------------------------|---------------------|-------------|---------|
| BDF / Noweda                 | Eucerinum W/O basis | 43430208WA  | 1       |
| BDF / Sanacorp               | Eucerinum W/O basis | 21430108WA  | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 541830108WA | 1       |
| beiersdorf                   | Eucerinum W/O basis | 24830208WA  | 1       |
| beiersdorf                   | Eucerinum W/O basis | 31230108WA  | 1       |
| beiersdorf                   | Eucerinum W/O basis | 94930108    | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 24830208WA  | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 21430108WA  | 2       |
| Beiersdorf                   | Eucerinum W/O basis | 32930208WA  | 5       |
| Beiersdorf                   | Eucerinum W/O basis | 31230108wa  | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 34930308WA  | 6       |
| Beiersdorf                   | Eucerinum W/O basis | 24072015A   | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 51630108WA  | 9       |
| 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  | 2       |
| Beiersdorf                   | Eucerinum W/O basis | 94930208    | 1       |
| Beiersdorf                   | Eucerinum W/O basis | 94930108    | 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       |
| 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       |

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| Supplier              | Substance                         | Batch       | Spectra |
|-----------------------|-----------------------------------|-------------|---------|
| 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               | 94930208    | 1       |
| Beiersdorf/Noweda     | Eucerinum W/O basis               | 94930108    | 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               | 21430108WA  | 1       |
| Caelo                 | Eucerinum W/O basis               | 41830108WA  | 3       |
| 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       |
| Geibo/Beiersdorf      | Eucerinum W/O basis               | 83730308WA  | 1       |
| Ichthyol-Gesellschaft | Eucerinum W/O basis               | 80330108WA  | 1       |
| Caelo                 | 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    | 2       |
| 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               | 80330108WA  | 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 <sup>®</sup> hydro cream | R011        | 1       |
| Alliance/Spirig       | Excipial <sup>®</sup> hydro cream | N043        | 1       |

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| Supplier                   | Substance                         | Batch            | Spectra |
|----------------------------|-----------------------------------|------------------|---------|
| Caelo                      | Excipial <sup>®</sup> hydro cream | LOT50782         | 1       |
| Caelo                      | Excipial <sup>®</sup> hydro cream | V031             | 1       |
| Caelo                      | Excipial <sup>®</sup> hydro cream | V071             | 2       |
| Caelo                      | Excipial <sup>®</sup> hydro cream | R045             | 1       |
| Chiesi/Phoenix             | Excipial <sup>®</sup> hydro cream | LOTV071          | 1       |
| Fa.Gehe                    | Excipial <sup>®</sup> hydro cream | 20160727Ma3      | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | S054             | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | T052             | 4       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | S041             | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | LOTV071          | 2       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | LOTV051          | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | V051             | 2       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | LOTV072          | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | 50782            | 3       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | 50634            | 2       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | 50564            | 1       |
| Galderma                   | Excipial <sup>®</sup> hydro cream | LOT50782         | 1       |
| Galderma /                 | Excipial <sup>®</sup> hydro cream | P28013-0         | 1       |
| Galderma / Noweda          | Excipial <sup>®</sup> hydro cream | T052             | 1       |
| Galderma / Phönix          | Excipial <sup>®</sup> hydro cream | LOTT052          | 2       |
| Galderma International/... | Excipial <sup>®</sup> hydro cream | 9767002          | 1       |
| Galderma/                  | Excipial <sup>®</sup> hydro cream | S012             | 1       |
| Galderma/                  | Excipial <sup>®</sup> hydro cream | V011             | 1       |
| Galderma/                  | Excipial <sup>®</sup> hydro cream | V011             | 1       |
| Galderma/ Gehe             | Excipial <sup>®</sup> hydro cream | V051             | 1       |
| Galderma/ Sana             | Excipial <sup>®</sup> hydro cream | S025             | 1       |
| Galderma/ Sana             | Excipial <sup>®</sup> hydro cream | S024             | 1       |
| Galderma/Alliance Healt... | Excipial <sup>®</sup> hydro cream | S025             | 1       |
| Galderma/Ebert             | Excipial <sup>®</sup> hydro cream | V041             | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> hydro cream | S024             | 2       |
| Galderma/Galderma          | Excipial <sup>®</sup> hydro cream | so25             | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> hydro cream | S054             | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> hydro cream | V051             | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> hydro cream | V042             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | R031             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | V042             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | V071             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | V072             | 2       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | 8767001          | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> hydro cream | 9767001          | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | S054             | 2       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | 170420EH/LOTT012 | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | 170706EH/LOTT091 | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | V042             | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | 180319EH/LOTV051 | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | V051             | 2       |
| Galderma/Noweda            | Excipial <sup>®</sup> hydro cream | 50564            | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | V031             | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 50235            | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | V071             | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 50515            | 2       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 50782            | 4       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 50634            | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 9767001          | 3       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 9767002          | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 9767005          | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> hydro cream | 767001           | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> hydro cream | V061             | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> hydro cream | S045             | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> hydro cream | S013             | 1       |

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| Supplier                      | Substance                         | Batch               | Spectra |
|-------------------------------|-----------------------------------|---------------------|---------|
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | V011                | 2       |
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | 50235               | 1       |
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | V071                | 1       |
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | 50782               | 4       |
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | 50515               | 1       |
| Galderma/Phönix               | Excipial <sup>®</sup> hydro cream | 9767005             | 1       |
| Galderma/Sanacorp             | Excipial <sup>®</sup> hydro cream | LOTV041             | 1       |
| Galderma/Würmi                | Excipial <sup>®</sup> hydro cream | R031                | 1       |
| Galderma/Würmtal-APO          | Excipial <sup>®</sup> hydro cream | S041                | 1       |
| Galderma-Spirig               | Excipial <sup>®</sup> hydro cream | To52-20171127Ma11   | 1       |
| Galderma-Spirig               | Excipial <sup>®</sup> hydro cream | V041-20180619Ma8    | 1       |
| Galderma-Spirig               | Excipial <sup>®</sup> hydro cream | 50235-E20190115Ma10 | 1       |
| Galderma-Spirig, Gehe 14. . . | Excipial <sup>®</sup> hydro cream | V061-20180830Ma11   | 1       |
| Gehe, Galderma Spirig         | Excipial <sup>®</sup> hydro cream | R031-20160615Ma7    | 1       |
| Gladerma/Ebert                | Excipial <sup>®</sup> hydro cream | V072                | 1       |
| Jenne                         | Excipial <sup>®</sup> hydro cream | S041                | 1       |
| Noweda                        | Excipial <sup>®</sup> hydro cream | 1120114             | 1       |
| Noweda                        | Excipial <sup>®</sup> hydro cream | V051                | 1       |
| Noweda/Galderma               | Excipial <sup>®</sup> hydro cream | T091                | 2       |
| Phoenix/Galderma              | Excipial <sup>®</sup> hydro cream | T012                | 1       |
| Phoenix/Spirig                | Excipial <sup>®</sup> hydro cream | M015                | 1       |
| Phoenix/Spirig                | Excipial <sup>®</sup> hydro cream | N044                | 1       |
| Phönix                        | Excipial <sup>®</sup> hydro cream | V011                | 1       |
| Phönix/Galderma               | Excipial <sup>®</sup> hydro cream | 9767005             | 1       |
| Phönix/Spirig                 | Excipial <sup>®</sup> hydro cream | N034                | 1       |
| Römerapo.                     | Excipial <sup>®</sup> hydro cream | R011                | 2       |
| Sanacorp                      | Excipial <sup>®</sup> hydro cream | LOTN011             | 1       |
| Sanacorp                      | Excipial <sup>®</sup> hydro cream | N011                | 1       |
| Spirig Pharma AG/ Anzag       | Excipial <sup>®</sup> hydro cream | LOTN034             | 1       |
| Spirig Pharma AG/ Anzag       | Excipial <sup>®</sup> hydro cream | LOTR013             | 1       |
| Spirig/Gehe                   | Excipial <sup>®</sup> hydro cream | R014                | 1       |
| spirig                        | Excipial <sup>®</sup> hydro cream | M014                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | M034                | 1       |
| spirig                        | Excipial <sup>®</sup> hydro cream | M041                | 6       |
| spirig                        | Excipial <sup>®</sup> hydro cream | 813993/10           | 1       |
| spirig                        | Excipial <sup>®</sup> hydro cream | N034                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | N014                | 1       |
| spirig                        | Excipial <sup>®</sup> hydro cream | N043                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | R013                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | N045                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | R014                | 2       |
| spirig                        | Excipial <sup>®</sup> hydro cream | s025                | 1       |
| Spirig                        | Excipial <sup>®</sup> hydro cream | K013                | 1       |
| Spirig                        | Excipial <sup>®</sup> hydro cream | N035                | 1       |
| Spirig                        | Excipial <sup>®</sup> hydro cream | N043                | 1       |
| Spirig                        | Excipial <sup>®</sup> hydro cream | R013                | 1       |
| Spirig                        | Excipial <sup>®</sup> hydro cream | S025                | 6       |
| Spirig (Galderma)             | Excipial <sup>®</sup> hydro cream | T012                | 2       |
| Spirig (Galderma)             | Excipial <sup>®</sup> hydro cream | T011                | 1       |
| Spirig (Galderma)             | Excipial <sup>®</sup> hydro cream | V011                | 2       |
| Spirig / Anzag                | Excipial <sup>®</sup> hydro cream | 813993/09           | 1       |
| Spirig / Anzag                | Excipial <sup>®</sup> hydro cream | 813993/10           | 1       |
| Spirig / Anzag                | Excipial <sup>®</sup> hydro cream | N034                | 1       |
| Spirig / Anzag                | Excipial <sup>®</sup> hydro cream | LOTN043             | 1       |
| Spirig / Gehe                 | Excipial <sup>®</sup> hydro cream | N011                | 1       |
| Spirig / Noweda               | Excipial <sup>®</sup> hydro cream | N035                | 1       |
| Spirig /Gehe                  | Excipial <sup>®</sup> hydro cream | LOTN044             | 1       |
| Spirig Pharma                 | Excipial <sup>®</sup> hydro cream | N013                | 1       |
| Spirig Pharma                 | Excipial <sup>®</sup> hydro cream | 813993/10           | 1       |
| Spirig Pharma                 | Excipial <sup>®</sup> hydro cream | N011                | 1       |

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| Supplier                   | Substance                         | Batch     | Spectra |
|----------------------------|-----------------------------------|-----------|---------|
| Spirig Pharma              | Excipial <sup>®</sup> hydro cream | LON014    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> hydro cream | N044      | 1       |
| Spirig Pharma AG           | Excipial <sup>®</sup> hydro cream | 813993/12 | 1       |
| Spirig Pharma AG           | Excipial <sup>®</sup> hydro cream | R025      | 5       |
| Spirig Pharma AG/GEHE      | Excipial <sup>®</sup> hydro cream | R011      | 1       |
| Spirig Pharma/ G           | Excipial <sup>®</sup> hydro cream | S053      | 1       |
| Spirig Pharma/ Noweda      | Excipial <sup>®</sup> hydro cream | N042      | 2       |
| Spirig/ Anzag              | Excipial <sup>®</sup> hydro cream | LOTM041   | 1       |
| Spirig/ Anzag              | Excipial <sup>®</sup> hydro cream | N035      | 1       |
| Spirig/ Fiebig             | Excipial <sup>®</sup> hydro cream | N013      | 1       |
| Spirig/ Gehe               | Excipial <sup>®</sup> hydro cream | M012      | 1       |
| Spirig/ Gehe               | Excipial <sup>®</sup> hydro cream | LOTR031   | 2       |
| Spirig/ Noweda             | Excipial <sup>®</sup> hydro cream | N043      | 3       |
| Spirig/ Noweda             | Excipial <sup>®</sup> hydro cream | 50782     | 1       |
| Spirig/ Phönix             | Excipial <sup>®</sup> hydro cream | R013      | 1       |
| Spirig/ Phönix             | Excipial <sup>®</sup> hydro cream | R014      | 1       |
| Spirig / Noweda            | Excipial <sup>®</sup> hydro cream | S041      | 5       |
| Alliance Healthcare        | Excipial <sup>®</sup> lipo cream  | M045      | 1       |
| Anzag/ Chiesi              | Excipial <sup>®</sup> lipo cream  | LOTR012   | 2       |
| Caelo                      | Excipial <sup>®</sup> lipo cream  | V051      | 1       |
| Caelo                      | Excipial <sup>®</sup> lipo cream  | 9031      | 1       |
| Caelo                      | Excipial <sup>®</sup> lipo cream  | 7121      | 1       |
| galderma                   | Excipial <sup>®</sup> lipo cream  | LOT50627  | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | N061      | 2       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | R026      | 2       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | R012      | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | R042      | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | R035      | 2       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | LOTS032   | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | T021      | 2       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | T061      | 2       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | v042      | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | LOTV041   | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | V091      | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | 50567     | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | 9769004   | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | 8769004   | 1       |
| Galderma                   | Excipial <sup>®</sup> lipo cream  | 9769010   | 1       |
| Galderma /AHD              | Excipial <sup>®</sup> lipo cream  | 50567     | 3       |
| Galderma /AHD              | Excipial <sup>®</sup> lipo cream  | 8769004   | 1       |
| Galderma International/... | Excipial <sup>®</sup> lipo cream  | 769002    | 1       |
| Galderma International/... | Excipial <sup>®</sup> lipo cream  | 769005    | 1       |
| Galderma/                  | Excipial <sup>®</sup> lipo cream  | 9769004   | 1       |
| Galderma/ Fiebig           | Excipial <sup>®</sup> lipo cream  | LOTV111   | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> lipo cream  | s023      | 6       |
| Galderma/ Noweda           | Excipial <sup>®</sup> lipo cream  | S031      | 9       |
| Galderma/ Noweda           | Excipial <sup>®</sup> lipo cream  | t022      | 5       |
| Galderma/ Noweda           | Excipial <sup>®</sup> lipo cream  | T022      | 4       |
| Galderma/ Noweda           | Excipial <sup>®</sup> lipo cream  | T021      | 5       |
| Galderma/ Sanacorp         | Excipial <sup>®</sup> lipo cream  | LOT50567  | 1       |
| Galderma/ Sanacorp         | Excipial <sup>®</sup> lipo cream  | 50567     | 1       |
| Galderma/ Sanacorp         | Excipial <sup>®</sup> lipo cream  | 8769004   | 1       |
| Galderma/AHCA              | Excipial <sup>®</sup> lipo cream  | 9769004   | 1       |
| Galderma/Alliance          | Excipial <sup>®</sup> lipo cream  | T061      | 1       |
| Galderma/Alliance          | Excipial <sup>®</sup> lipo cream  | V091      | 2       |
| Galderma/Alliance          | Excipial <sup>®</sup> lipo cream  | V112      | 1       |
| Galderma/Alliance          | Excipial <sup>®</sup> lipo cream  | 769002    | 1       |
| Galderma/Alliance          | Excipial <sup>®</sup> lipo cream  | 769013    | 2       |
| Galderma/Anzag             | Excipial <sup>®</sup> lipo cream  | S011      | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> lipo cream  | R026      | 1       |

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| Supplier                  | Substance                        | Batch            | Spectra |
|---------------------------|----------------------------------|------------------|---------|
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | ro26             | 1       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | R042             | 9       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | S023             | 8       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | T021             | 8       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | V121             | 1       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | 50567            | 1       |
| Galderma/Galderma         | Excipial <sup>®</sup> lipo cream | 8769004          | 1       |
| Galderma/Gehe             | Excipial <sup>®</sup> lipo cream | R042             | 2       |
| Galderma/Gehe             | Excipial <sup>®</sup> lipo cream | V091             | 1       |
| Galderma/Gehe             | Excipial <sup>®</sup> lipo cream | 50849            | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | R011             | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | R026             | 2       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | 170420EL/LOTT021 | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | T021             | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | 171819E/LOTT021  | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | 180208L/L0TV091  | 1       |
| Galderma/Noweda           | Excipial <sup>®</sup> lipo cream | 50567            | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | R042             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | R026             | 2       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | R012             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | S031             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | S023             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | S032             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | T021             | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 50627            | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 50567            | 6       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 9769004          | 3       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 8769004          | 1       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 9769011          | 6       |
| Galderma/Phönix           | Excipial <sup>®</sup> lipo cream | 9769010          | 1       |
| Galderma/Phönix WE: 03... | Excipial <sup>®</sup> lipo cream | L0TV012          | 1       |
| Galderma/Würmtalapo       | Excipial <sup>®</sup> lipo cream | R042             | 2       |
| Gameda Noweda             | Excipial <sup>®</sup> lipo cream | 180504EL/L0TV112 | 1       |
| Gehe                      | Excipial <sup>®</sup> lipo cream | N061             | 1       |
| Gehe/Galderma             | Excipial <sup>®</sup> lipo cream | L0TS031          | 1       |
| Noweda                    | Excipial <sup>®</sup> lipo cream | 50627            | 1       |
| Noweda                    | Excipial <sup>®</sup> lipo cream | 9769030          | 1       |
| Noweda/ Galderma          | Excipial <sup>®</sup> lipo cream | V112180607EL     | 1       |
| Caelo                     | Excipial <sup>®</sup> lipo cream | L0TS023          | 1       |
| Phoenix/Galderma          | Excipial <sup>®</sup> lipo cream | 50567            | 1       |
| Phönix/Galderma           | Excipial <sup>®</sup> lipo cream | S023             | 1       |
| Sanacorp                  | Excipial <sup>®</sup> lipo cream | M027             | 1       |
| Sanacorp                  | Excipial <sup>®</sup> lipo cream | L0TN016          | 1       |
| spirig                    | Excipial <sup>®</sup> lipo cream | M017             | 1       |
| spirig                    | Excipial <sup>®</sup> lipo cream | M016             | 4       |
| spirig                    | Excipial <sup>®</sup> lipo cream | 813994/09        | 1       |
| spirig                    | Excipial <sup>®</sup> lipo cream | M042             | 2       |
| spirig                    | Excipial <sup>®</sup> lipo cream | N018             | 4       |
| spirig                    | Excipial <sup>®</sup> lipo cream | N021             | 5       |
| spirig                    | Excipial <sup>®</sup> lipo cream | R012             | 3       |
| spirig                    | Excipial <sup>®</sup> lipo cream | N061             | 3       |
| spirig                    | Excipial <sup>®</sup> lipo cream | r042             | 1       |
| Spirig                    | Excipial <sup>®</sup> lipo cream | K021             | 1       |
| Spirig                    | Excipial <sup>®</sup> lipo cream | N021             | 1       |
| Spirig                    | Excipial <sup>®</sup> lipo cream | R012             | 4       |
| Spirig (Galderma)         | Excipial <sup>®</sup> lipo cream | T061             | 1       |
| Spirig / Anzag            | Excipial <sup>®</sup> lipo cream | 813994/09        | 1       |
| Spirig / Anzag            | Excipial <sup>®</sup> lipo cream | M017             | 1       |
| Spirig / Anzag            | Excipial <sup>®</sup> lipo cream | N018             | 3       |
| Spirig / Anzag            | Excipial <sup>®</sup> lipo cream | M042             | 3       |

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| Supplier                     | Substance                         | Batch       | Spectra |
|------------------------------|-----------------------------------|-------------|---------|
| Spirig / Anzag               | Excipial <sup>®</sup> lipo cream  | N018        | 1       |
| Spirig / Anzag               | Excipial <sup>®</sup> lipo cream  | LOTN021     | 2       |
| Spirig / Gehe                | Excipial <sup>®</sup> lipo cream  | LOTN021     | 2       |
| Spirig / Gehe                | Excipial <sup>®</sup> lipo cream  | LOTR012     | 1       |
| Spirig / Gehe                | Excipial <sup>®</sup> lipo cream  | R012        | 1       |
| Spirig Pharma                | Excipial <sup>®</sup> lipo cream  | 813994/09   | 2       |
| Spirig Pharma                | Excipial <sup>®</sup> lipo cream  | T021        | 1       |
| Spirig Pharma AG             | Excipial <sup>®</sup> lipo cream  | M042        | 1       |
| Spirig Pharma AG/Allian. ... | Excipial <sup>®</sup> lipo cream  | N018        | 1       |
| Spirig Pharma AG/GEHE        | Excipial <sup>®</sup> lipo cream  | R012        | 1       |
| Spirig Pharma Europe GmbH    | Excipial <sup>®</sup> lipo cream  | R026        | 1       |
| Spirig/AHD                   | Excipial <sup>®</sup> lipo cream  | M017        | 1       |
| Spirig/AHD                   | Excipial <sup>®</sup> lipo cream  | N018        | 2       |
| Spirig/AHD                   | Excipial <sup>®</sup> lipo cream  | V112        | 3       |
| Spirig/Anzag                 | Excipial <sup>®</sup> lipo cream  | S023        | 1       |
| Spirig/Anzag                 | Excipial <sup>®</sup> lipo cream  | S031        | 1       |
| Spirig/Anzag                 | Excipial <sup>®</sup> lipo cream  | R011        | 1       |
| Spirig/Gehe                  | Excipial <sup>®</sup> lipo cream  | R012        | 1       |
| Spirig/Gehe                  | Excipial <sup>®</sup> lipo cream  | R026        | 1       |
| Spirig/Otto                  | Excipial <sup>®</sup> lipo cream  | 50627       | 1       |
| Spirig/Phoenix               | Excipial <sup>®</sup> lipo cream  | M041        | 2       |
| Spirig/Phoenix               | Excipial <sup>®</sup> lipo cream  | M042        | 2       |
| Spirig/Phönix                | Excipial <sup>®</sup> lipo cream  | 4622        | 1       |
| Spirig/Phönix                | Excipial <sup>®</sup> lipo cream  | R012        | 2       |
| Spirig/Phönix                | Excipial <sup>®</sup> lipo cream  | R042        | 1       |
| Wolff                        | Excipial <sup>®</sup> lipo cream  | S031        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | R186        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | V101        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | V143        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | S206        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | LotV137     | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | R167        | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | LoTV143     | 1       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | 173048      | 2       |
| Caelo                        | Excipial <sup>®</sup> U Lipolotio | S073        | 1       |
| Caesar & Loretz GmbH         | Excipial <sup>®</sup> U Lipolotio | 19065102    | 1       |
| Dermapharm                   | Excipial <sup>®</sup> U Lipolotio | 169010      | 1       |
| Euro/ Phönix                 | Excipial <sup>®</sup> U Lipolotio | 4417A-03749 | 1       |
| Fagron                       | Excipial <sup>®</sup> U Lipolotio | N168        | 2       |
| Fagron                       | Excipial <sup>®</sup> U Lipolotio | V081        | 1       |
| Fiebig                       | Excipial <sup>®</sup> U Lipolotio | T061        | 2       |
| Fiebig/DR.Wolf               | Excipial <sup>®</sup> U Lipolotio | V028        | 1       |
| Fiebig/Galderma              | Excipial <sup>®</sup> U Lipolotio | V101        | 1       |
| Fischar                      | Excipial <sup>®</sup> U Lipolotio | LOTN085     | 1       |
| Galaderma                    | Excipial <sup>®</sup> U Lipolotio | R072        | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | V011        | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | LOT50249    | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | LOT50842    | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 174756      | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 173469      | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 303485      | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 318718      | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 309994      | 1       |
| Galaderma/Krieger            | Excipial <sup>®</sup> U Lipolotio | 318628      | 1       |
| Galaderma/Phönix             | Excipial <sup>®</sup> U Lipolotio | V041        | 1       |
| Galaderma/Phönix             | Excipial <sup>®</sup> U Lipolotio | LOTV152     | 1       |
| galderma                     | Excipial <sup>®</sup> U Lipolotio | R024        | 1       |
| Galderma                     | Excipial <sup>®</sup> U Lipolotio | R111        | 1       |
| Galderma                     | Excipial <sup>®</sup> U Lipolotio | R167        | 2       |
| Galderma                     | Excipial <sup>®</sup> U Lipolotio | R168        | 1       |

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| Supplier                   | Substance                         | Batch          | Spectra |
|----------------------------|-----------------------------------|----------------|---------|
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | S064           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | S091           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | R171           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | S137           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | R172           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | S147           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | T056           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | L0TS123        | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | T125           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | S148           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | L0TV121        | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V139           | 2       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V153           | 2       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V159           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V101           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V053           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 50458          | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | V152           | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 50688          | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 50346          | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 50852          | 6       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 270918A        | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 169853         | 2       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 169005         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 170615         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 173469         | 2       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 174756         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 305489         | 2       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 310709         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 308637         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 311839         | 1       |
| Galderma                   | Excipial <sup>®</sup> U Lipolotio | 319748         | 1       |
| Galderma (Spirig Pharma... | Excipial <sup>®</sup> U Lipolotio | R061           | 1       |
| Galderma (Spirig Pharma... | Excipial <sup>®</sup> U Lipolotio | T057           | 1       |
| Galderma / Noweda          | Excipial <sup>®</sup> U Lipolotio | V152           | 1       |
| Galderma / Noweda          | Excipial <sup>®</sup> U Lipolotio | T115           | 1       |
| Galderma / Galderma        | Excipial <sup>®</sup> U Lipolotio | R086           | 1       |
| Galderma / Kehr            | Excipial <sup>®</sup> U Lipolotio | R171           | 1       |
| Galderma / Kehr            | Excipial <sup>®</sup> U Lipolotio | R167           | 1       |
| Galderma / Kehr            | Excipial <sup>®</sup> U Lipolotio | T029           | 2       |
| Galderma / Noweda          | Excipial <sup>®</sup> U Lipolotio | T073/170522EUL | 1       |
| Galderma /AHD              | Excipial <sup>®</sup> U Lipolotio | 169853         | 1       |
| Galderma /Fiebig           | Excipial <sup>®</sup> U Lipolotio | 170615         | 2       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | V121           | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 50876          | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 171711         | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 167638         | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 173041         | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 314142         | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Lipolotio | 319748         | 1       |
| Galderma Labor.            | Excipial <sup>®</sup> U Lipolotio | 169010         | 1       |
| Galderma Labor.            | Excipial <sup>®</sup> U Lipolotio | 169110         | 1       |
| Galderma Labor.            | Excipial <sup>®</sup> U Lipolotio | 310709         | 2       |
| Galderma Labor.            | Excipial <sup>®</sup> U Lipolotio | 312811         | 1       |
| Galderma, Sanacorp         | Excipial <sup>®</sup> U Lipolotio | L0TS042        | 1       |
| Galderma/                  | Excipial <sup>®</sup> U Lipolotio | 319921         | 1       |
| Galderma/ Alliance         | Excipial <sup>®</sup> U Lipolotio | T115           | 1       |
| Galderma/ Fiebig           | Excipial <sup>®</sup> U Lipolotio | 830071/17      | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | T072           | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | L0T50450       | 1       |

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| Supplier                   | Substance                         | Batch             | Spectra |
|----------------------------|-----------------------------------|-------------------|---------|
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 50876             | 2       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 169110            | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 312417            | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 174756            | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 319844            | 1       |
| Galderma/ Noweda           | Excipial <sup>®</sup> U Lipolotio | 326881            | 1       |
| Galderma/ NOWEDA           | Excipial <sup>®</sup> U Lipolotio | V082              | 1       |
| Galderma/AEP               | Excipial <sup>®</sup> U Lipolotio | V165              | 1       |
| Galderma/Alliance Healt... | Excipial <sup>®</sup> U Lipolotio | T121              | 1       |
| Galderma/Anzag             | Excipial <sup>®</sup> U Lipolotio | R183              | 1       |
| Galderma/Anzag             | Excipial <sup>®</sup> U Lipolotio | S206              | 1       |
| Galderma/Fiebig            | Excipial <sup>®</sup> U Lipolotio | V062              | 1       |
| Galderma/Fiebig            | Excipial <sup>®</sup> U Lipolotio | 319844            | 2       |
| galderma/G                 | Excipial <sup>®</sup> U Lipolotio | L0TS202           | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> U Lipolotio | s017              | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> U Lipolotio | S017              | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> U Lipolotio | S142              | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> U Lipolotio | 50852             | 1       |
| Galderma/Galderma          | Excipial <sup>®</sup> U Lipolotio | 174960            | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | R189              | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | T061              | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | T066              | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | S139              | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | T156              | 2       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | V108              | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | L0T50450          | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 50450             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 50691             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 50842             | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 171710            | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 169831            | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 312417            | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Lipolotio | 332540            | 1       |
| Galderma/Graf-Eberhard...  | Excipial <sup>®</sup> U Lipolotio | 174966            | 1       |
| Galderma/Graf-Eberhard...  | Excipial <sup>®</sup> U Lipolotio | 310709            | 1       |
| Galderma/Kehr              | Excipial <sup>®</sup> U Lipolotio | S071              | 1       |
| Galderma/Kehr              | Excipial <sup>®</sup> U Lipolotio | S203              | 1       |
| Galderma/Kehr              | Excipial <sup>®</sup> U Lipolotio | 320973            | 1       |
| Galderma/Krieger           | Excipial <sup>®</sup> U Lipolotio | 50689             | 3       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 170420EUL/L0TS204 | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 170518EUL/L0TT073 | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 170316EL/L0TT073  | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | V011              | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | V041              | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 170906EL/T072     | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | V141              | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 50689             | 2       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 50842             | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | V082              | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | V143              | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 314142            | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 319844            | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Lipolotio | 320973            | 1       |
| Galderma/phoenix           | Excipial <sup>®</sup> U Lipolotio | 169847            | 1       |
| Galderma/phoenix           | Excipial <sup>®</sup> U Lipolotio | 169010            | 1       |
| Galderma/phoenix           | Excipial <sup>®</sup> U Lipolotio | 171711            | 3       |
| Galderma/phoenix           | Excipial <sup>®</sup> U Lipolotio | 310709            | 5       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | L0TT085           | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 3717E-03749       | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | V041              | 1       |

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| Supplier                   | Substance                         | Batch   | Spectra |
|----------------------------|-----------------------------------|---------|---------|
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | V061    | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | V011    | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 50450   | 1       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 175042  | 2       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 308637  | 2       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 312417  | 2       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 314603  | 2       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 319422  | 3       |
| Galderma/Phoenix           | Excipial <sup>®</sup> U Lipolotio | 319748  | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | T116    | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | V041    | 2       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | V136    | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 50876   | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 50569   | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 170615  | 4       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 174756  | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 173469  | 4       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 309994  | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 314603  | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 319748  | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Lipolotio | 326881  | 2       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | V073    | 1       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | V103    | 2       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | V038    | 1       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | V151    | 1       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | 167638  | 1       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | 311839  | 2       |
| Galderma/Sanacorp          | Excipial <sup>®</sup> U Lipolotio | 319351  | 1       |
| Galderma/Spirig Pharma AG  | Excipial <sup>®</sup> U Lipolotio | L0TR187 | 1       |
| Galderma/Würmtal Apotheke  | Excipial <sup>®</sup> U Lipolotio | S132    | 2       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | R142    | 1       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | S071    | 4       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | S205    | 2       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | T149    | 1       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | V142    | 1       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | 50852   | 1       |
| Galderma/Würmtal-Apotheke  | Excipial <sup>®</sup> U Lipolotio | 169010  | 1       |
| Dermapharm                 | Excipial <sup>®</sup> U Lipolotio | 311839  | 1       |
| Galderma/Anzag             | Excipial <sup>®</sup> U Lipolotio | 171710  | 1       |
| Gehe                       | Excipial <sup>®</sup> U Lipolotio | S132    | 1       |
| Gehe                       | Excipial <sup>®</sup> U Lipolotio | S143    | 1       |
| Gehe                       | Excipial <sup>®</sup> U Lipolotio | V152    | 1       |
| Gehe                       | Excipial <sup>®</sup> U Lipolotio | V121    | 1       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 50459   | 1       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 50688   | 1       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 50890   | 2       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 174996  | 1       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 174966  | 1       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 309197  | 2       |
| GEHE                       | Excipial <sup>®</sup> U Lipolotio | 312811  | 1       |
| Caelo                      | Excipial <sup>®</sup> U Lipolotio | L0TS081 | 1       |
| Gehe/Galderma              | Excipial <sup>®</sup> U Lipolotio | LotV011 | 1       |
| GEHE/GALDERMA 25_11:16     | Excipial <sup>®</sup> U Lipolotio | S147    | 1       |
| Gehe-Spring                | Excipial <sup>®</sup> U Lipolotio | L0TR167 | 1       |
| Kehr/Galderma              | Excipial <sup>®</sup> U Lipolotio | T029    | 1       |
| Nestle skin health         | Excipial <sup>®</sup> U Lipolotio | 174966  | 1       |
| Nestle Skin Health         | Excipial <sup>®</sup> U Lipolotio | 174756  | 1       |
| Nestle Skin Health/ Now... | Excipial <sup>®</sup> U Lipolotio | 314142  | 1       |
| Nestle Skin Health/Gehe    | Excipial <sup>®</sup> U Lipolotio | 174756  | 1       |
| Nestle Skin Health/Noweda  | Excipial <sup>®</sup> U Lipolotio | 305489  | 2       |

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| Supplier                   | Substance                         | Batch   | Spectra |
|----------------------------|-----------------------------------|---------|---------|
| Nestle Skin Health/Phönix  | Excipial <sup>®</sup> U Lipolotio | 303485  | 1       |
| Nestle Skin Health/Phönix  | Excipial <sup>®</sup> U Lipolotio | 311839  | 1       |
| Nestle Skin Health/Sana... | Excipial <sup>®</sup> U Lipolotio | 319344  | 1       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | R261    | 1       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | 305489  | 1       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | 311839  | 2       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | 319844  | 1       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | 312811  | 2       |
| Noweda                     | Excipial <sup>®</sup> U Lipolotio | 327343  | 1       |
| Caelo                      | Excipial <sup>®</sup> U Lipolotio | S203    | 1       |
| Caelo                      | Excipial <sup>®</sup> U Lipolotio | 50569   | 1       |
| Noweda/Galderma            | Excipial <sup>®</sup> U Lipolotio | 174756  | 1       |
| Noweda/Galderma            | Excipial <sup>®</sup> U Lipolotio | V121    | 1       |
| Phoenix                    | Excipial <sup>®</sup> U Lipolotio | N105    | 1       |
| Phoenix                    | Excipial <sup>®</sup> U Lipolotio | S091    | 1       |
| Phoenix                    | Excipial <sup>®</sup> U Lipolotio | S138    | 2       |
| Phoenix                    | Excipial <sup>®</sup> U Lipolotio | S148    | 1       |
| Phoenix                    | Excipial <sup>®</sup> U Lipolotio | 319748  | 1       |
| Phoenix WE 16.01.17 EK...  | Excipial <sup>®</sup> U Lipolotio | LOTS122 | 2       |
| Phoenix/Spirig             | Excipial <sup>®</sup> U Lipolotio | N041    | 1       |
| PHÖNIX                     | Excipial <sup>®</sup> U Lipolotio | T063    | 1       |
| PHÖNIX                     | Excipial <sup>®</sup> U Lipolotio | V039    | 1       |
| PHÖNIX                     | Excipial <sup>®</sup> U Lipolotio | V105    | 1       |
| sanacorp / Nestle          | Excipial <sup>®</sup> U Lipolotio | 174800  | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | N086    | 1       |
| spirig                     | Excipial <sup>®</sup> U Lipolotio | M142    | 1       |
| spirig                     | Excipial <sup>®</sup> U Lipolotio | N013    | 1       |
| spirig                     | Excipial <sup>®</sup> U Lipolotio | N058    | 3       |
| spirig                     | Excipial <sup>®</sup> U Lipolotio | N086    | 1       |
| spirig                     | Excipial <sup>®</sup> U Lipolotio | R037    | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | M091    | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | N123    | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | R047    | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | LOTT057 | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | 50450   | 1       |
| Spirig                     | Excipial <sup>®</sup> U Lipolotio | 169838  | 1       |
| Spirig / Anzag             | Excipial <sup>®</sup> U Lipolotio | M182    | 1       |
| Spirig / Anzag             | Excipial <sup>®</sup> U Lipolotio | N032    | 1       |
| Spirig / Anzag             | Excipial <sup>®</sup> U Lipolotio | N041    | 1       |
| Spirig / Galderma / Anzag  | Excipial <sup>®</sup> U Lipolotio | 170615  | 1       |
| Spirig / Galderma / Anzag  | Excipial <sup>®</sup> U Lipolotio | 169010  | 1       |
| Spirig / Sanacorp          | Excipial <sup>®</sup> U Lipolotio | R041    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | LOTK131 | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | LOTN013 | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | M134    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | S122    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | V082    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | V053    | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Lipolotio | V141    | 2       |
| Spirig Pharma / Noweda     | Excipial <sup>®</sup> U Lipolotio | S141    | 1       |
| Spirig Pharma/Kehr         | Excipial <sup>®</sup> U Lipolotio | T156    | 2       |
| Spirig/ Noweda             | Excipial <sup>®</sup> U Lipolotio | S225    | 1       |
| Spirig/AHD                 | Excipial <sup>®</sup> U Lipolotio | M085    | 1       |
| Spirig/AHD                 | Excipial <sup>®</sup> U Lipolotio | N058    | 1       |
| Spirig/AHD                 | Excipial <sup>®</sup> U Lipolotio | lotno86 | 1       |
| Spirig/Fiebig              | Excipial <sup>®</sup> U Lipolotio | S143    | 1       |
| Spirig/Galderma            | Excipial <sup>®</sup> U Lipolotio | R156    | 2       |
| Spirig/Galderma            | Excipial <sup>®</sup> U Lipolotio | R146    | 1       |
| Spirig/Gehe                | Excipial <sup>®</sup> U Lipolotio | M102    | 2       |

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| Supplier                  | Substance                           | Batch    | Spectra |
|---------------------------|-------------------------------------|----------|---------|
| Spirig/Gehe               | Excipial <sup>®</sup> U Lipolotio   | M146     | 1       |
| Spirig/Gehe               | Excipial <sup>®</sup> U Lipolotio   | M182     | 1       |
| Spirig/Gehe               | Excipial <sup>®</sup> U Lipolotio   | R114     | 1       |
| Spirig/Gehe               | Excipial <sup>®</sup> U Lipolotio   | R262     | 1       |
| Spirig/Kehr               | Excipial <sup>®</sup> U Lipolotio   | V038     | 1       |
| Spirig/Noweda             | Excipial <sup>®</sup> U Lipolotio   | N061     | 1       |
| Spirig/Phönix             | Excipial <sup>®</sup> U Lipolotio   | R033     | 1       |
| Spirig/Würmtal-Apotheke   | Excipial <sup>®</sup> U Lipolotio   | R145     | 2       |
| Sprig (Galderma)/ G       | Excipial <sup>®</sup> U Lipolotio   | S123     | 1       |
| Galaderma/Krieger         | Excipial <sup>®</sup> U10 Lipolotio | T071     | 1       |
| Galderma                  | Excipial <sup>®</sup> U10 Lipolotio | LOT50679 | 1       |
| Galderma                  | Excipial <sup>®</sup> U10 Lipolotio | 304231   | 1       |
| Galderma/AHCA             | Excipial <sup>®</sup> U10 Lipolotio | LOT50604 | 1       |
| Galderma/Alliance         | Excipial <sup>®</sup> U10 Lipolotio | T042     | 1       |
| Galderma/Galderma         | Excipial <sup>®</sup> U10 Lipolotio | 308310   | 1       |
| Galderma/Krieger          | Excipial <sup>®</sup> U10 Lipolotio | 50581    | 3       |
| Galderma/Krieger          | Excipial <sup>®</sup> U10 Lipolotio | 308310   | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | V092     | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 169759   | 2       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 50679    | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 308601   | 3       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 320154   | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 321879   | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 322729   | 1       |
| Galderma/Sanacorp         | Excipial <sup>®</sup> U10 Lipolotio | 323868   | 1       |
| Galderma/Würmtal-Apo.     | Excipial <sup>®</sup> U10 Lipolotio | T053     | 1       |
| Galderma/Würmtal-Apotheke | Excipial <sup>®</sup> U10 Lipolotio | V042     | 1       |
| Spirig/AHD                | Excipial <sup>®</sup> U10 Lipolotio | M025     | 1       |
| Artesan                   | Fabitop <sup>®</sup> base cream     | GLWW5    | 1       |
| Artesan                   | Fabitop <sup>®</sup> base cream     | GLWD4    | 1       |
| Caelo                     | Fabitop <sup>®</sup> base cream     | glwd2    | 1       |
| Caelo                     | Fabitop <sup>®</sup> base cream     | GWWL3    | 1       |
| Fontapharm                | Fabitop <sup>®</sup> base cream     | GLWW4    | 1       |
| Fontapharm                | Fabitop <sup>®</sup> base cream     | GLWD2    | 9       |
| Fontapharm                | Fabitop <sup>®</sup> base cream     | GLWD2x2  | 1       |
| Fontapharm                | Fabitop <sup>®</sup> base cream     | 101601   | 1       |
| Fontapharm                | Fabitop <sup>®</sup> base cream     | GLWD3    | 2       |
| fontapharm AG             | Fabitop <sup>®</sup> base cream     | 101601   | 1       |
| Fontapharm/Gehe           | Fabitop <sup>®</sup> base cream     | GLWD4    | 1       |
| Fontapharm/Noweda         | Fabitop <sup>®</sup> base cream     | GLWD3    | 1       |
| Fontapharm/Noweda         | Fabitop <sup>®</sup> base cream     | 101601   | 1       |
| Fontapharm/Phönix         | Fabitop <sup>®</sup> base cream     | 101601   | 7       |
| Fontapharm/Sanacop        | Fabitop <sup>®</sup> base cream     | 101601   | 3       |
| Spangropharm              | Fabitop <sup>®</sup> base cream     | 1016022  | 1       |
| Fontapharma AG / Noweda   | Fabitop <sup>®</sup> base cream     | 1016021  | 1       |
| Gehe                      | Fabitop <sup>®</sup> base cream     | GRWW2    | 6       |
| Jenne                     | Fabitop <sup>®</sup> base cream     | GWWL1    | 1       |
| jenne artisan             | Fabitop <sup>®</sup> base cream     | GLWWW5   | 1       |
| Caelo                     | Fabitop <sup>®</sup> base cream     | GWWL1    | 1       |
| Phoenix/Artesan           | Fabitop <sup>®</sup> base cream     | GLWD5    | 3       |
| Phönix                    | Fabitop <sup>®</sup> base cream     | GLWD3    | 1       |
| Phönix Fontapharm         | Fabitop <sup>®</sup> base cream     | 101601   | 1       |
| Phönix/Fontapharm         | Fabitop <sup>®</sup> base cream     | GRWW2    | 1       |
| THC/Noweda                | Fabitop <sup>®</sup> 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       |

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| Supplier                     | Substance                    | Batch    | Spectra |
|------------------------------|------------------------------|----------|---------|
| Galderma                     | Lipoderm <sup>®</sup> lotion | R044     | 2       |
| Galderma                     | Lipoderm <sup>®</sup> lotion | S021     | 1       |
| Galderma                     | Lipoderm <sup>®</sup> lotion | T011     | 1       |
| Galderma                     | Lipoderm <sup>®</sup> lotion | 169310   | 1       |
| Galderma/Alliance            | Lipoderm <sup>®</sup> lotion | LOTV012  | 2       |
| Galderma/Alliance            | Lipoderm <sup>®</sup> lotion | 50316    | 2       |
| Galderma/AllianceHC          | Lipoderm <sup>®</sup> lotion | T011     | 2       |
| Galderma/Kehr                | Lipoderm <sup>®</sup> lotion | S021     | 2       |
| Galderma/Phoenix             | Lipoderm <sup>®</sup> lotion | S041     | 1       |
| Galderma/Phönix              | Lipoderm <sup>®</sup> lotion | T043     | 1       |
| Hedinger/Noweda              | Lipoderm <sup>®</sup> lotion | 169310   | 1       |
| Ichthyol/Phönix              | Lipoderm <sup>®</sup> lotion | LOTT043  | 1       |
| Jenne                        | Lipoderm <sup>®</sup> lotion | T011     | 1       |
| Nestle Skin Health           | Lipoderm <sup>®</sup> lotion | 169310   | 1       |
| Noweda                       | Lipoderm <sup>®</sup> lotion | 169310   | 1       |
| spirig                       | Lipoderm <sup>®</sup> lotion | 4622     | 1       |
| Spirig                       | Lipoderm <sup>®</sup> lotion | R011     | 2       |
| Spirig                       | Lipoderm <sup>®</sup> lotion | LOTR011  | 1       |
| Spirig                       | Lipoderm <sup>®</sup> lotion | R023     | 2       |
| Spirig                       | Lipoderm <sup>®</sup> lotion | S041     | 2       |
| Spirig Pharma                | Lipoderm <sup>®</sup> lotion | V012     | 1       |
| Spirig Pharma AG             | Lipoderm <sup>®</sup> lotion | N041     | 1       |
| Spirig Pharma AG/Allian. ... | Lipoderm <sup>®</sup> lotion | N041     | 1       |
| Spirig Pharma AG/Allian. ... | Lipoderm <sup>®</sup> lotion | R011     | 4       |
| Spirig Pharma AG/Allian. ... | Lipoderm <sup>®</sup> lotion | N041     | 1       |
| Spirig Pharma AG/Allian. ... | Lipoderm <sup>®</sup> lotion | R023     | 8       |
| Spirig Pharma AG/Allian. ... | Lipoderm <sup>®</sup> lotion | R044     | 3       |
| Spirig Pharma/Phoenix        | Lipoderm <sup>®</sup> lotion | T043     | 2       |
| Spirig/AHD                   | Lipoderm <sup>®</sup> lotion | N041     | 1       |
| Spirig/AHD                   | Lipoderm <sup>®</sup> lotion | LOTN041  | 1       |
| Spirig/AllianceHC            | Lipoderm <sup>®</sup> lotion | S021     | 3       |
| Spirig/Gehe                  | Lipoderm <sup>®</sup> lotion | S041     | 1       |
| Spirig/Phoenix               | Lipoderm <sup>®</sup> lotion | M065     | 4       |
| SpirigPharm/Noweda           | Lipoderm <sup>®</sup> lotion | LOT50932 | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY02804  | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY02H20  | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY02L84  | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY02TTH  | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY0431K  | 1       |
| AHD                          | Neribas <sup>®</sup> cream   | YY0431J  | 1       |
| Bayer/ Sanacorp              | Neribas <sup>®</sup> cream   | YY002L6  | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | yyo18ff  | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | YY01X64  | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | YY0203H  | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | yy01kk7  | 1       |
| Chiesi / Gehe                | Neribas <sup>®</sup> cream   | 32097A   | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | yy01k94  | 1       |
| Caelo                        | Neribas <sup>®</sup> cream   | yy0203H  | 1       |
| GP GmbH/Spangro              | Neribas <sup>®</sup> cream   | Y018FF   | 1       |
| GPGrenzach Produktion/P...   | Neribas <sup>®</sup> cream   | YY01673  | 1       |
| Intendis / Gehe              | Neribas <sup>®</sup> cream   | 21076A   | 1       |
| Intendis / Sanacorp          | Neribas <sup>®</sup> cream   | 24105A   | 1       |
| Intendis GmbH                | Neribas <sup>®</sup> cream   | 24089A   | 1       |
| Jenapharm                    | Neribas <sup>®</sup> cream   | 33100C   | 1       |
| Jenapharm                    | Neribas <sup>®</sup> cream   | YY0203H  | 1       |
| Jenapharm                    | Neribas <sup>®</sup> cream   | YY02805  | 2       |
| Jenapharm                    | Neribas <sup>®</sup> cream   | YY0277H  | 1       |
| Jenapharm / Gehe             | Neribas <sup>®</sup> cream   | 34104C   | 1       |
| Jenapharm / Gehe             | Neribas <sup>®</sup> cream   | YY02L84  | 1       |
| Jenapharm / Noweda           | Neribas <sup>®</sup> cream   | YY02H20  | 2       |

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| Supplier              | Substance                                 | Batch      | Spectra |
|-----------------------|-------------------------------------------|------------|---------|
| Jenapharm / Sanacorp  | Neribas <sup>®</sup> cream                | YY02804    | 1       |
| Jenapharm / Noweda    | Neribas <sup>®</sup> cream                | YY00C34    | 1       |
| Jenapharm/            | Neribas <sup>®</sup> cream                | YY01KK7    | 1       |
| Jenapharm/ G          | Neribas <sup>®</sup> cream                | YY01KK7    | 1       |
| Jenapharm/ Noweda     | Neribas <sup>®</sup> cream                | YY00216    | 1       |
| Jenapharm/ Noweda     | Neribas <sup>®</sup> cream                | YY01TCN    | 1       |
| Jenapharm/Alliance    | Neribas <sup>®</sup> cream                | YY000C3    | 2       |
| Jenapharm/Alliance    | Neribas <sup>®</sup> cream                | YY001HS    | 1       |
| Jenapharm/Alliance    | Neribas <sup>®</sup> cream                | YY006LX    | 1       |
| Jenapharm/gehe        | Neribas <sup>®</sup> cream                | yy02805    | 1       |
| Jenapharm/Gehe        | Neribas <sup>®</sup> cream                | YY006KY    | 1       |
| Jenapharm/Gehe        | Neribas <sup>®</sup> cream                | YY005HT    | 1       |
| Jenapharm/Gehe        | Neribas <sup>®</sup> cream                | YY01KK7    | 1       |
| Jenapharm/Krieger     | Neribas <sup>®</sup> cream                | YY02805    | 1       |
| Jenapharm/Krieger     | Neribas <sup>®</sup> cream                | YY02H20    | 1       |
| Jenapharm/Noweda      | Neribas <sup>®</sup> cream                | YY00C35    | 2       |
| Jenapharm/Noweda      | Neribas <sup>®</sup> cream                | YY00XEF    | 2       |
| Jenapharm/Noweda      | Neribas <sup>®</sup> cream                | YY014NJ    | 2       |
| Jenapharm/Noweda      | Neribas <sup>®</sup> cream                | YY01CXP    | 2       |
| Jenapharm/Phoenix     | Neribas <sup>®</sup> cream                | YY023J5    | 1       |
| Jenapharm/Phönix      | Neribas <sup>®</sup> cream                | YY02H20    | 1       |
| Karo Pharma           | Neribas <sup>®</sup> cream                | YY04EYL    | 1       |
| Karopharm/Krieger     | Neribas <sup>®</sup> cream                | YY0431K    | 1       |
| Krieger               | Neribas <sup>®</sup> cream                | 3388       | 1       |
| Leo Pharma/Krieger    | Neribas <sup>®</sup> cream                | YY0431J    | 1       |
| LEO Pharma/Phönix     | Neribas <sup>®</sup> cream                | YY0431K    | 1       |
| LEO Pharma/Phönix     | Neribas <sup>®</sup> cream                | YY04EYL    | 1       |
| Leopharm              | Neribas <sup>®</sup> cream                | YY02TTH    | 1       |
| Caelo                 | Neribas <sup>®</sup> cream                | yy02805    | 1       |
| Noweda/Jenapharm      | Neribas <sup>®</sup> cream                | YY00PF1    | 1       |
| Noweda/Leopharm       | Neribas <sup>®</sup> cream                | YY02H20    | 1       |
| Phoenix               | Neribas <sup>®</sup> cream                | 3094       | 1       |
| Phoenix               | Neribas <sup>®</sup> cream                | 3229       | 1       |
| Phoenix               | Neribas <sup>®</sup> cream                | 3378       | 1       |
| Phönix                | Neribas <sup>®</sup> cream                | 3139       | 1       |
| Phönix / Jenapharm    | Neribas <sup>®</sup> cream                | YY01FX3    | 1       |
| Römer/apo             | Neribas <sup>®</sup> cream                | YY005HT    | 2       |
| Caelo                 | Neuroderm <sup>®</sup> moisturising cream | 6051801    | 1       |
| Infectopharm/Gehe     | Neuroderm <sup>®</sup> moisturising cream | S0315081   | 1       |
| Allergika Pharma GmbH | Allergika <sup>®</sup> Base cream         |            | 1       |
| Chiesi                | Asche Basis <sup>®</sup> cream            | 24220A     | 2       |
| Chiesi GmbH/Gehe      | Asche Basis <sup>®</sup> cream            |            | 2       |
| Chiesi,Fa.Gehe        | Asche Basis <sup>®</sup> cream            |            | 1       |
| Chiesi,Gehe           | Asche Basis <sup>®</sup> cream            |            | 1       |
| Chiesi/Krieger        | Asche Basis <sup>®</sup> cream            |            | 1       |
| Dr.Wolff              | Asche Basis <sup>®</sup> cream            |            | 1       |
| Chiesi                | Asche Basis <sup>®</sup> lotion           | 24049A     | 1       |
| Chiesi                | Asche Basis <sup>®</sup> lotion           | 64082A     | 1       |
| KoKo GmbH/KoKo GmbH   | DMS <sup>®</sup> base cream classic       |            | 1       |
| Beiersdorf            | Eucerinum O/W basis                       | 41830108WA | 3       |
| Beiersdorf            | Eucerinum O/W basis                       | 53430208WA | 4       |
| Beiersdorf            | Eucerinum W/O basis                       | 31230108WA | 1       |
| Beiersdorf            | Eucerinum W/O basis                       | 83730208WA | 6       |
| Spirig Pharma/Gehe    | Excipial <sup>®</sup> hydro cream         |            | 1       |
| Spirig/Gehe           | Excipial <sup>®</sup> hydro cream         |            | 3       |
| Alliance Healthcare   | Excipial <sup>®</sup> lipo cream          |            | 2       |
| spirig                | Excipial <sup>®</sup> lipo cream          |            | 1       |
| Fontapharm            | Fabitop <sup>®</sup> base cream           | GLWD5      | 1       |
|                       | Neribas <sup>®</sup> cream                | YY02H20    | 1       |
| Caelo                 | Neuroderm <sup>®</sup> moisturising cream |            | 3       |

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| Supplier                   | Substance                                 | Batch | Spectra |
|----------------------------|-------------------------------------------|-------|---------|
| Gehe                       | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Infecto/Phönix             | Neuroderm <sup>®</sup> moisturising cream |       | 2       |
| infectopharm               | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Infectopharm               | Neuroderm <sup>®</sup> moisturising cream |       | 6       |
| InfectoPharm               | Neuroderm <sup>®</sup> moisturising cream |       | 17      |
| Infectopharm/Alliance      | Neuroderm <sup>®</sup> moisturising cream |       | 4       |
| Infectopharm/Fiebig        | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Infectopharm/Kehr          | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Infectopharm/noweda        | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Infectopharm/Noweda        | Neuroderm <sup>®</sup> moisturising cream |       | 3       |
| Infectopharm/Phoenix       | Neuroderm <sup>®</sup> moisturising cream |       | 2       |
| Infectopharm/Phönix        | Neuroderm <sup>®</sup> moisturising cream |       | 8       |
| InfectoPharma/Alliance ... | Neuroderm <sup>®</sup> moisturising cream |       | 2       |
| Infetopharm                | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Noweda                     | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Bombastus                  | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| PHÖNIX                     | Neuroderm <sup>®</sup> moisturising cream |       | 1       |
| Sanacorp                   | Neuroderm <sup>®</sup> moisturising cream |       | 1       |

- 6734 spectra from 740 *Apo-Ident* customers from a total of 2703 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 3510          | 0              | 21 195        |
| <b>Type B</b> | 0              | 2105          | 115            | 18 051        |
| <b>Type C</b> | 0              | 2401          | 160            | 6708          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.8291 %) |
| <b>Type B</b> | 100.0000 % (> 99.9440 %) | 94.8198 % (> 94.6847 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8030 %) | 93.7524 % (> 93.6353 %)  |

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

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

Where the number of spectra does 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                | 11.29                  | —                              |
| Dimeticone ointment 10% SR                     | 12.87                  | —                              |
| Optiderm <sup>®</sup> lotion                   | 15.25                  | —                              |
| Dexeryl <sup>®</sup>                           | 15.51                  | —                              |
| Neuroderm <sup>®</sup> moisturising cream lipo | 15.59                  | —                              |
| La Roche-Posay Toleriane                       | 18.88                  | —                              |
| Allergika evening primrose oil cream 20%       | 24.74                  | —                              |
| Amciderm <sup>®</sup> Base cream               | 28.06                  | —                              |
| Linola <sup>®</sup> Sept                       | 33.37                  | —                              |
| Dermifant <sup>®</sup> kids cream              | 34.94                  | —                              |
| Dermatop <sup>®</sup> base ointment            | 35.80                  | —                              |
| Nourivan <sup>™</sup> Antiox                   | 40.98                  | —                              |
| Linola <sup>®</sup> H fat N                    | 60.59                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30634     | 30634               | 0.00                         | 39.04                           |
| 30635     | 30635               | 0.00                         | 37.03                           |
| 30713     | 30713               | 0.00                         | 45.61                           |
| 30722     | 30722               | 0.00                         | 35.36                           |
| 30725     | 30725               | 0.00                         | 50.32                           |
| 30726     | 30726               | 0.00                         | 35.79                           |
| 30732     | 30732               | 0.00                         | 41.58                           |
| 30733     | 30733               | 0.00                         | 34.11                           |
| 30775     | 30775               | 0.00                         | 54.89                           |
| 30828     | 30828               | 0.00                         | 20.89                           |
| 30845     | 30845               | 0.00                         | 16.01                           |
| 30993     | 30993               | 0.00                         | 42.86                           |
| 31041     | 31041               | 0.00                         | 20.09                           |
| 31050     | 31050               | 0.00                         | 43.41                           |
| 31058     | 31058               | 0.00                         | 41.72                           |
| 31061     | 31061               | 0.00                         | 42.83                           |
| 31066     | 31066               | 0.00                         | 30.85                           |
| 31067     | 31067               | 0.00                         | 39.95                           |
| 31068     | 31068               | 0.00                         | 26.82                           |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31070            | 31070                      | 0.00                                | 18.96                                  |
| 31072            | 31072                      | 0.00                                | 40.27                                  |
| 31082            | 31082                      | 0.00                                | 60.15                                  |
| 31085            | 31085                      | 0.00                                | 54.98                                  |
| 31088            | 31088                      | 0.00                                | 46.86                                  |
| 31089            | 31089                      | 0.00                                | 46.53                                  |
| 31095            | 31095                      | 0.00                                | 45.45                                  |
| 31102            | 31102                      | 0.00                                | 44.00                                  |
| 31115            | 31115                      | 0.00                                | 34.98                                  |
| 31234            | 31234                      | 0.00                                | 34.26                                  |
| 31236            | 31236                      | 0.00                                | 38.35                                  |
| 31280            | 31280                      | 0.00                                | 45.89                                  |
| 31281            | 31281                      | 0.00                                | 30.43                                  |
| 31307            | 31307                      | 0.00                                | 15.37                                  |
| 31308            | 31308                      | 0.00                                | 46.07                                  |
| 31309            | 31309                      | 0.00                                | 49.53                                  |
| 31511            | 31511                      | 0.00                                | 49.57                                  |
| 31520            | 31520                      | 0.00                                | 49.22                                  |
| 31535            | 31535                      | 0.00                                | 36.14                                  |
| 31539            | 31539                      | 0.00                                | 20.96                                  |
| 31576            | 31576                      | 0.00                                | 60.85                                  |
| 31578            | 31578                      | 0.00                                | 31.89                                  |
| 31627            | 31627                      | 0.00                                | 19.05                                  |
| 31730            | 31730                      | 0.00                                | 26.62                                  |
| 31761            | 31761                      | 0.00                                | 41.75                                  |
| 31772            | 31772                      | 0.00                                | 19.65                                  |
| 31869            | 31869                      | 0.00                                | 15.25                                  |
| 31870            | 31870                      | 0.00                                | 45.57                                  |
| 31873            | 31873                      | 0.00                                | 26.16                                  |
| 31874            | 31874                      | 0.00                                | 50.60                                  |
| 31950            | 31950                      | 0.00                                | 19.63                                  |
| 32177            | 32177                      | 0.00                                | 32.91                                  |
| 32178            | 32178                      | 0.00                                | 42.02                                  |
| 32767            | 32767                      | 0.00                                | 41.85                                  |
| 32916            | 32916                      | 0.00                                | 42.57                                  |
| 32997            | 32997                      | 0.00                                | 40.55                                  |
| 33039            | 33039                      | 0.00                                | 19.53                                  |
| 33194            | 33194                      | 0.00                                | 32.87                                  |
| 33195            | 33195                      | 0.00                                | 34.11                                  |
| 33207            | 33207                      | 0.00                                | 45.62                                  |
| 33208            | 33208                      | 0.00                                | 45.03                                  |
| 33213            | 33213                      | 0.00                                | 25.61                                  |
| 33221            | 33221                      | 0.00                                | 42.37                                  |
| 33270            | 33270                      | 0.00                                | 41.51                                  |
| 33636            | 33636                      | 0.00                                | 44.74                                  |
| 33668            | 33668                      | 0.00                                | 44.90                                  |
| 33669            | 33669                      | 0.00                                | 43.26                                  |
| 33737            | 33737                      | 0.00                                | 24.22                                  |
| 33793            | 33793                      | 0.00                                | 16.36                                  |
| 33968            | 33968                      | 0.00                                | 42.13                                  |
| 33969            | 33969                      | 0.00                                | 41.43                                  |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 34043            | 34043                      | 0.00                                | 49.03                                  |
| 34044            | 34044                      | 0.00                                | 21.49                                  |
| 34117            | 34117                      | 0.00                                | 33.39                                  |
| 34119            | 34119                      | 0.00                                | 23.53                                  |
| 34359            | 34359                      | 0.00                                | 39.58                                  |
| 34360            | 34360                      | 0.00                                | 16.28                                  |
| 35149            | 35149                      | 0.00                                | 13.52                                  |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Immortelle oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30450-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 449 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       |

- 9290 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 5             | 0              | 9290          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8109 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------------|---------------------------|-----------------------------------|
| Melissa oil               | 15.17                     | —                                 |
| Ginger oil                | 15.86                     | —                                 |
| Vetiver bourbon oil       | 21.48                     | —                                 |
| Lemon grass oil           | 24.68                     | —                                 |
| Citrus oil                | 29.80                     | —                                 |
| Myrtle oil                | 30.96                     | —                                 |
| Cedar wood oil            | 33.62                     | —                                 |
| Chamomile (essential oil) | 34.62                     | —                                 |
| Spearmint oil             | 39.88                     | —                                 |
| Swiss pine oil            | 41.14                     | —                                 |
| Patchouli oil             | 44.75                     | —                                 |
| Marjoram oil              | 46.34                     | —                                 |
| Cypress oil               | 46.41                     | —                                 |
| Carrot seed oil           | 47.29                     | —                                 |
| Hyssop oil                | 48.99                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31138     | 31138                  | 0.00                            | 25.27                              |
| 32069     | 32069                  | 0.00                            | 20.67                              |
| 33727     | 33727                  | 0.00                            | 29.24                              |
| 34383     | 34383                  | 0.00                            | 27.27                              |

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 2.4-2021-02

Validated substance/substance group **Juniper oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31559-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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       |

- 9293 spectra from 772 *Apo-Ident* customers from a total of 3673 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 77            | 43             | 20 841        |
| <b>Type C</b> | 0              | 2             | 0              | 9293          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 64.1667 % (> 61.6667 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8304 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Dwarf pine oil      | 21.47                     | —                                 |
| Spearmint oil       | 23.27                     | —                                 |
| Frankincense oil    | 25.64                     | —                                 |
| Spruce needle oil   | 28.31                     | —                                 |
| Angelica root oil   | 29.53                     | —                                 |
| Swiss pine oil      | 35.29                     | —                                 |
| Pine silvestris oil | 36.60                     | —                                 |
| Silver fir oil      | 43.43                     | —                                 |
| Citrus oil          | 45.20                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31559     | 31559                  | 0.00                            | 24.23                              |
| 31687     | 31687                  | 0.00                            | 25.88                              |
| 32809     | 32809                  | 0.00                            | 21.94                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>La Roche-Posay Cold Cream Naturel</b>                        |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30829-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group         | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 449 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... | 54M11P    | 1       |
| La Roche-Posay             | La Roche-Posay Cold Cream Na... | 54M91P    | 1       |
| La Roche-Posay             | La Roche-Posay Cold Cream Na... | 54M01P    | 1       |
| Mea-SanacorpWE10.02.201... | La Roche-Posay Cold Cream Na... | LOT54M91P | 1       |

- 9290 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 5             | 0              | 9290          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8109 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------------------------------------|---------------------------|-----------------------------------|
| Stomahesive <sup>®</sup> adhesive paste | 50.66                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30829     | 30829                  | 0.00                            | 80.20                              |
| 31074     | 31074                  | 0.00                            | 83.65                              |
| 31765     | 31765                  | 0.00                            | 82.88                              |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>La Roche-Posay Toleriane</b>                                 |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30827-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group | 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 54 961 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.
- 24 585 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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       |

- 9288 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 24 585        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 6             | 1              | 9288          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8072 %) | 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                           | 17.69                  | —                              |
| Neuroderm <sup>®</sup> moisturising cream     | 21.27                  | —                              |
| Excipial <sup>®</sup> U10 Lipolotio           | 22.65                  | —                              |
| DMS <sup>®</sup> base cream high classic      | 24.26                  | —                              |
| Base cream Taoasis                            | 27.67                  | —                              |
| DMS <sup>®</sup> base cream classic           | 27.83                  | —                              |
| Hans Karrer Lipocream MicroSilver             | 28.04                  | —                              |
| Abitima <sup>®</sup> clinic body cream        | 28.95                  | —                              |
| Asche Basis <sup>®</sup> lotion               | 29.69                  | —                              |
| Excipial <sup>®</sup> U Lipolotio             | 29.86                  | —                              |
| Lipoderm <sup>®</sup> lotion                  | 31.74                  | —                              |
| Dimeticone ointment 10% SR                    | 35.00                  | —                              |
| Asche Basis <sup>®</sup> cream                | 35.60                  | —                              |
| Neribas <sup>®</sup> cream                    | 40.36                  | —                              |
| Hans Karrer Lipolotion MicroSilver            | 42.13                  | —                              |
| Neuroderm <sup>®</sup> care lotion            | 42.20                  | —                              |
| Linola <sup>®</sup> body milk                 | 42.62                  | —                              |
| DMS <sup>®</sup> base cream high classic plus | 42.90                  | —                              |
| Excipial <sup>®</sup> hydro cream             | 51.45                  | —                              |

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                         | 31.03                           |
| 31094     | 31094               | 0.00                         | 25.49                           |
| 32563     | 32563               | 0.00                         | 30.75                           |

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 2.4-2021-02

Validated substance/substance group **Lemon grass oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30661-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Lemon grass oil; Cymbopogonis 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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 130930-115336  | 1       |
| Taoasis            | Lemon grass oil | 8911011-121890 | 1       |
| Taoasis            | Lemon grass oil | FFL457-123568  | 1       |
| Taoasis            | Lemon grass oil | 18988-125876   | 1       |
| Taoasis            | Lemon grass oil | 1448-126624    | 1       |
| Taoasis            | Lemon grass oil | 1663-125423    | 1       |
| Taoasis            | Lemon grass oil | 1448-128742    | 1       |
| Taoasis            | Lemon grass oil | 1777-2776      | 1       |
| Taoasis            | Lemon grass oil | 17004202       | 1       |
| Taoasis            | Lemon grass oil | 1448-507       | 1       |
| Taoasis            | Lemon grass oil | 6093-6119      | 1       |

- 9277 spectra from 772 *Apo-Ident* customers from a total of 3658 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 119           | 1              | 20 841        |
| <b>Type C</b> | 0              | 18            | 0              | 9277          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 99.1667 % (> 96.6667 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8015 %) | 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       | 29.18                  | –                              |
| Carrot seed oil     | 30.42                  | –                              |
| Cypress oil         | 32.71                  | –                              |
| Immortelle oil      | 34.13                  | –                              |
| Marjoram oil        | 34.87                  | –                              |
| Tea tree oil        | 40.41                  | –                              |
| Myrtle oil          | 40.71                  | –                              |
| Ginger oil          | 40.93                  | –                              |
| Melissa oil         | 44.95                  | –                              |
| Vetiver bourbon oil | 48.19                  | –                              |
| Citrus oil          | 52.69                  | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30661     | 30661               | 0.00                         | 39.05                           |
| 31185     | 31185               | 0.00                         | 31.65                           |
| 31187     | 31187               | 0.00                         | 29.18                           |
| 31549     | 31549               | 0.00                         | 36.94                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Liniment ointments**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30731-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Liniment ointments; Amciderm<sup>®</sup> Base cream; Excipial<sup>®</sup> U Hydrolotio; Linola<sup>®</sup> O/W cream; Linola<sup>®</sup> Sept; Nourivan<sup>™</sup> 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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Liniment ointments        | 15     | 5      | 34     |

## 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 <sup>®</sup> Base c... | 313311           | 31509     | 60      | not required |
| Almirall      | Amciderm <sup>®</sup> Base c... | 313311           | 31628     | 75      | not required |
| Almirall      | Amciderm <sup>®</sup> Base c... | 650341           | 33502     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> U Hydr... | M016             | 30731     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> U Hydr... | M063             | 31073     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> U Hydr... | N013             | 31279     | 40      | not required |
| Spirig Pharma | Excipial <sup>®</sup> U Hydr... | R014             | 31536     | 60      | not required |
| Dr. Wolff     | Linola <sup>®</sup> O/W cream   | 238482           | 30834     | 40      | not required |
| Dr. Wolff     | Linola <sup>®</sup> O/W cream   | 334010           | 31133     | 40      | not required |
| Dr. Wolff     | Linola <sup>®</sup> O/W cream   | 432480           | 31312     | 40      | not required |
| Dr. Wolff     | Linola <sup>®</sup> Sept        | 334080           | 31079     | 40      | not required |
| Dr. Wolff     | Linola <sup>®</sup> Sept        | 509361           | 31856     | 60      | not required |
| Dr. Wolff     | Linola <sup>®</sup> Sept        | 707990           | 34126     | 40      | not required |
| Fagron        | Nourivan <sup>TM</sup> Antiox   | 14C11-T09-010959 | 31495     | 60      | not required |
| Fagron        | Nourivan <sup>TM</sup> Antiox   | 1503258          | 31958     | 45      | not required |
| Fagron        | Nourivan <sup>TM</sup> Antiox   | 1703842          | 33789     | 30      | not required |

## Validation samples

A total of 54 961 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.
- 23 955 spectra from a total of 495 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 <sup>†</sup>. The following applies to the remaining unmarked samples:



In the same batch, there 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 <sup>®</sup> Base cream   | 538331  | 32758              | 40      |
| Almirall      | Amciderm <sup>®</sup> Base cream   | 822351  | 34365              | 40      |
| Spirig Pharma | Excipial <sup>®</sup> U Hydrolotio | S061    | 33206              | 40      |
| Spirig Pharma | Excipial <sup>®</sup> U Hydrolotio | V052    | 33981              | 40      |
| Dr. Wolff     | Linola <sup>®</sup> Sept           | 603190  | 32760              | 40      |
| Dr. Wolff     | Linola <sup>®</sup> Sept           | 603190  | 33257              | 40      |
| Fagron        | Nourivan <sup>TM</sup> Antiox      | 1503258 | 31958 <sup>†</sup> | 15      |
| Fagron        | Nourivan <sup>TM</sup> Antiox      | 1503258 | 32778              | 40      |
| Fagron        | Nourivan <sup>TM</sup> Antiox      | 1503258 | 32822              | 40      |
| Fagron        | Nourivan <sup>TM</sup> Antiox      | 1703842 | 33789 <sup>†</sup> | 10      |

- 20 616 spectra from a total of 444 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.

- 218 spectra from 73 *Apo-Ident* customers from 118 batches from the substance/substance group *Liniment ointments*.
- Among them are spectra of independent samples from 111 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier          | Substance                          | Batch    | Spectra |
|-------------------|------------------------------------|----------|---------|
| Allmiral/Gehe     | Amciderm <sup>®</sup> Base cream   | 418321   | 1       |
| Almirall/Alliance | Amciderm <sup>®</sup> Base cream   | 650341   | 1       |
| Almirall/Phönix   | Amciderm <sup>®</sup> Base cream   | 538331   | 3       |
| Almirall/Phönix   | Amciderm <sup>®</sup> Base cream   | 822351   | 2       |
| Almirall/Phönix   | Amciderm <sup>®</sup> Base cream   | 12161    | 1       |
| Fagron            | Amciderm <sup>®</sup> Base cream   | 23102017 | 1       |
| Caelo             | Excipial <sup>®</sup> U Hydrolotio | L0TR092  | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | L0TR054  | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | T011     | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | 172481   | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | V042     | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | 50857    | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | 1107483  | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | 302972   | 1       |
| Galderma          | Excipial <sup>®</sup> U Hydrolotio | 306123   | 1       |

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<sup>†</sup>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 <sup>®</sup> U Hydrolotio | 318203          | 1       |
| Galderma International/... | Excipial <sup>®</sup> U Hydrolotio | V042            | 1       |
| Galderma/ Fiebig           | Excipial <sup>®</sup> U Hydrolotio | L0TV022         | 1       |
| Galderma/ Gehe             | Excipial <sup>®</sup> U Hydrolotio | L0TR053         | 1       |
| Galderma/ Phoenix/ 07.1... | Excipial <sup>®</sup> U Hydrolotio | 302972          | 1       |
| Galderma/ Phoenix/ 09.0... | Excipial <sup>®</sup> U Hydrolotio | 327533          | 1       |
| Galderma/Alliance          | Excipial <sup>®</sup> U Hydrolotio | T072            | 2       |
| Galderma/Alliance          | Excipial <sup>®</sup> U Hydrolotio | 50723           | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Hydrolotio | S014            | 1       |
| Galderma/Gehe              | Excipial <sup>®</sup> U Hydrolotio | 50723           | 1       |
| Galderma/Noweda            | Excipial <sup>®</sup> U Hydrolotio | R054            | 1       |
| Galderma/P                 | Excipial <sup>®</sup> U Hydrolotio | V051            | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Hydrolotio | T013            | 1       |
| Galderma/Phönix            | Excipial <sup>®</sup> U Hydrolotio | V011            | 1       |
| Nestle/ Phönix             | Excipial <sup>®</sup> U Hydrolotio | 331554          | 2       |
| Noweda                     | Excipial <sup>®</sup> U Hydrolotio | S061            | 1       |
| Phoenix/Spirig             | Excipial <sup>®</sup> U Hydrolotio | M016            | 1       |
| PHÖNIX                     | Excipial <sup>®</sup> U Hydrolotio | V051            | 1       |
| PHÖNIX                     | Excipial <sup>®</sup> U Hydrolotio | 50593           | 1       |
| Phönix, Galderma, 09.04... | Excipial <sup>®</sup> U Hydrolotio | 317160          | 1       |
| SANACORP                   | Excipial <sup>®</sup> U Hydrolotio | 172141          | 1       |
| Spirig                     | Excipial <sup>®</sup> U Hydrolotio | N013            | 1       |
| Spirig                     | Excipial <sup>®</sup> U Hydrolotio | N013            | 1       |
| Spirig Pharma              | Excipial <sup>®</sup> U Hydrolotio | N033            | 1       |
| Spirig Pharma AG/ NOWEDA   | Excipial <sup>®</sup> U Hydrolotio | L0TN022         | 1       |
| Spirig Pharma AG/Noweda    | Excipial <sup>®</sup> U Hydrolotio | R054            | 1       |
| Spirig/Gehe                | Excipial <sup>®</sup> U Hydrolotio | R054            | 3       |
| AHD                        | Linola <sup>®</sup> O/W cream      | 437110          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 1111111111      | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 905070          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 239181          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 238520          | 2       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 238484          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 330760          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 606100          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 438350          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 236281          | 1       |
| Caelo                      | Linola <sup>®</sup> O/W cream      | 238530          | 2       |
| chiesi / Noweda            | Linola <sup>®</sup> O/W cream      | 331460          | 1       |
| Defektur                   | Linola <sup>®</sup> O/W cream      | 438350          | 1       |
| Dr Wolff/ Sanacorp         | Linola <sup>®</sup> O/W cream      | 808420          | 1       |
| Dr Wolff/ Sanacorp         | Linola <sup>®</sup> O/W cream      | 810150          | 2       |
| Dr. August Wolff GmbH &... | Linola <sup>®</sup> O/W cream      | 903600          | 1       |
| Dr. August Wolff GmbH &... | Linola <sup>®</sup> O/W cream      | 904680          | 1       |
| Dr. August Wolff GmbH &... | Linola <sup>®</sup> O/W cream      | 908380          | 1       |
| Dr. August Wolff GmbH &... | Linola <sup>®</sup> O/W cream      | 170522LC/701090 | 1       |
| Dr. August Wolff GmbH&C... | Linola <sup>®</sup> O/W cream      | 808420          | 1       |
| Dr. August Wolff GmbH&C... | Linola <sup>®</sup> O/W cream      | 901150          | 2       |
| Dr. August Wolff GmbH&C... | Linola <sup>®</sup> O/W cream      | 908930          | 1       |
| Dr. August Wolff GmbH&C... | Linola <sup>®</sup> O/W cream      | 904890          | 2       |
| Dr. August Wolff GmbH&C... | Linola <sup>®</sup> O/W cream      | 1750            | 1       |
| Dr. August Wolff/ Jenne    | Linola <sup>®</sup> O/W cream      | 1090            | 1       |
| Dr. Wolf/GEHE              | Linola <sup>®</sup> O/W cream      | 437110          | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 236290          | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 238520          | 2       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 238484          | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 233200          | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 238530          | 2       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 435080          | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream      | 431200          | 3       |

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| <b>Supplier</b>           | <b>Substance</b>              | <b>Batch</b> | <b>Spectra</b> |
|---------------------------|-------------------------------|--------------|----------------|
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 434430       | 3              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 435530       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 437120       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 438200       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 505280       | 4              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 504100       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 508280       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 505200       | 4              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 512330       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 602300       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 510792       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 602190       | 3              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 510430       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 605419       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 606121       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 605410       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 904810       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 901150       | 1              |
| DR. WOLFF                 | Linola <sup>®</sup> O/W cream | 234192       | 1              |
| Dr. Wolff 25.03.2013 S... | Linola <sup>®</sup> O/W cream | 236290       | 3              |
| Dr. Wolff / Gehe          | Linola <sup>®</sup> O/W cream | 338990       | 3              |
| Dr. Wolff / Sanacorp      | Linola <sup>®</sup> O/W cream | 905070       | 1              |
| Dr. Wolff GmbH / Phoenix  | Linola <sup>®</sup> O/W cream | 606100       | 1              |
| Dr. Wolff/ Jenne          | Linola <sup>®</sup> O/W cream | 904680       | 1              |
| Dr. Wolff/ Noweda         | Linola <sup>®</sup> O/W cream | 901150       | 1              |
| Dr. Wolff/Gehe            | Linola <sup>®</sup> O/W cream | 434320       | 2              |
| Dr. Wolff/Gehe            | Linola <sup>®</sup> O/W cream | 138350       | 1              |
| Dr. Wolff/Malteser        | Linola <sup>®</sup> O/W cream | 330751       | 1              |
| Dr. Wolff/Malteser        | Linola <sup>®</sup> O/W cream | 333880       | 1              |
| Dr. Wolff/Malteser        | Linola <sup>®</sup> O/W cream | 338990       | 1              |
| Dr. Wolff/Noweda          | Linola <sup>®</sup> O/W cream | 438360       | 1              |
| Dr. August Wolff          | Linola <sup>®</sup> O/W cream | 233140       | 1              |
| Dr. August Wolff          | Linola <sup>®</sup> O/W cream | 607140       | 1              |
| Dr. August Wolff          | Linola <sup>®</sup> O/W cream | 605560       | 1              |
| Dr. August Wolff          | Linola <sup>®</sup> O/W cream | 505560       | 1              |
| Dr. August Wolff/Ebert    | Linola <sup>®</sup> O/W cream | 333640       | 2              |
| Dr. August Wolff/Ebert    | Linola <sup>®</sup> O/W cream | 431250       | 1              |
| Dr. August Wolff/Ebert    | Linola <sup>®</sup> O/W cream | 432970       | 1              |
| Dr. August Wolff/Kehr     | Linola <sup>®</sup> O/W cream | 9525         | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 238482       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 238530       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 334003       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 333640       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 432490       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 438200       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 438360       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 607140       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 807360       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 808420       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 903600       | 1              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 901150       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 904890       | 3              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 908630       | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 10520        | 2              |
| Dr. Wolff                 | Linola <sup>®</sup> O/W cream | 910420       | 1              |
| DR. Wolff                 | Linola <sup>®</sup> O/W cream | 1490         | 3              |
| DR. Wolff                 | Linola <sup>®</sup> O/W cream | 908930       | 1              |
| DR. Wolff                 | Linola <sup>®</sup> O/W cream | 7060         | 1              |
| DR. Wolff                 | Linola <sup>®</sup> O/W cream | 11410        | 1              |
| Dr. Wolff / Phö           | Linola <sup>®</sup> O/W cream | 908930       | 1              |

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| Supplier                   | Substance                     | Batch   | Spectra |
|----------------------------|-------------------------------|---------|---------|
| Dr. Wolff / Phö            | Linola <sup>®</sup> O/W cream | 910420  | 2       |
| Dr. Wolff/ Anzag           | Linola <sup>®</sup> O/W cream | 234193  | 1       |
| Dr. Wolff/Anzag            | Linola <sup>®</sup> O/W cream | 238520  | 2       |
| Dr. Wolff/Fiebig           | Linola <sup>®</sup> O/W cream | 510430  | 1       |
| Dr. Wolff/Fiebig           | Linola <sup>®</sup> O/W cream | 606120  | 1       |
| Dr. Wolff/Gehe             | Linola <sup>®</sup> O/W cream | 238520  | 1       |
| Dr. Wolff/Gehe             | Linola <sup>®</sup> O/W cream | 432490  | 2       |
| Dr. Wolff/Gehe             | Linola <sup>®</sup> O/W cream | 438360  | 1       |
| Dr. Wolff/Gehe             | Linola <sup>®</sup> O/W cream | 606100  | 1       |
| Dr. Wolff/Noweda           | Linola <sup>®</sup> O/W cream | 233200  | 1       |
| Dr. Wolff/Phoenix          | Linola <sup>®</sup> O/W cream | 903600  | 1       |
| Dr. Wolff/Phoenix          | Linola <sup>®</sup> O/W cream | 904680  | 1       |
| Euro OTC                   | Linola <sup>®</sup> O/W cream | 333730  | 1       |
| Gehe                       | Linola <sup>®</sup> O/W cream | 607140  | 1       |
| Gehe/Dr Wolff              | Linola <sup>®</sup> O/W cream | 903600  | 1       |
| Hedinger                   | Linola <sup>®</sup> O/W cream | 908930  | 1       |
| Infectopharm Sanacorp      | Linola <sup>®</sup> O/W cream | 810780  | 1       |
| Phö/Dr. Wolff              | Linola <sup>®</sup> O/W cream | 901100  | 1       |
| Phoenix/Wolff              | Linola <sup>®</sup> O/W cream | 333640  | 1       |
| wolff                      | Linola <sup>®</sup> O/W cream | 434320  | 1       |
| Wolff / Gehe               | Linola <sup>®</sup> O/W cream | 431130  | 3       |
| Wolff / Noweda             | Linola <sup>®</sup> O/W cream | 431120  | 4       |
| Wolff GmbH/Sanacorp        | Linola <sup>®</sup> O/W cream | 903540  | 1       |
| Wolff/ Sanacorp            | Linola <sup>®</sup> O/W cream | 908930  | 1       |
| Wolff/Sanacorp             | Linola <sup>®</sup> O/W cream | 333630  | 2       |
| Fagron                     | Nourivan <sup>TM</sup> Antiox | 150325  | 1       |
| Dr. August Wolff GmbH &... | Linola <sup>®</sup> O/W cream |         | 1       |
| Dr. Wolff                  | Linola <sup>®</sup> O/W cream | 432480  | 1       |
| Fagron                     | Nourivan <sup>TM</sup> Antiox | 1503258 | 3       |

- 9077 spectra from 772 *Apo-Ident* customers from a total of 3567 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 750           | 0              | 23 955        |
| <b>Type B</b> | 0              | 307           | 38             | 20 484        |
| <b>Type C</b> | 0              | 214           | 4              | 9076          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.2000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9449 %) | 88.9855 % (> 88.1159 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8184 %) | 98.1651 % (> 96.7890 %)  |

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

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

Where the number of spectra does 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<br>main model | Distance in<br>second-stage model |
|-----------------------------------------------|---------------------------|-----------------------------------|
| Hans Karrer Hydrocream MicroSilver            | 10.84                     | —                                 |
| Sebexol <sup>®</sup> basic pH 5 formula basis | 11.37                     | —                                 |
| Sebexol <sup>®</sup> cream lotion pH 5        | 15.87                     | —                                 |
| Dimeticone ointment 10% SR                    | 17.48                     | —                                 |
| Wofacutan wash lotion                         | 19.58                     | —                                 |
| Abitima <sup>®</sup> clinic face cream        | 21.18                     | —                                 |
| Base cream Taoasis                            | 23.34                     | —                                 |
| Optiderm <sup>®</sup> lotion                  | 30.50                     | —                                 |
| Hans Karrer Lipolotion MicroSilver            | 30.92                     | —                                 |
| Neuroderm <sup>®</sup> moisturising cream     | 32.24                     | —                                 |
| Asche Basis <sup>®</sup> lotion               | 36.19                     | —                                 |
| Eucerinum W/O basis                           | 39.31                     | —                                 |
| Excipial <sup>®</sup> U10 Lipolotio           | 40.46                     | —                                 |
| Fabitop <sup>®</sup> base cream               | 40.74                     | —                                 |
| Fenistil <sup>®</sup> Gel                     | 43.63                     | —                                 |
| DMS <sup>®</sup> base cream classic           | 48.35                     | —                                 |
| DMS <sup>®</sup> base cream high classic      | 50.79                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30731     | 30731                  | 0.00                            | 10.83                              |
| 30834     | 30834                  | 0.00                            | 30.43                              |
| 31073     | 31073                  | 0.00                            | 10.54                              |
| 31079     | 31079                  | 0.00                            | 30.56                              |
| 31133     | 31133                  | 0.00                            | 30.92                              |
| 31279     | 31279                  | 0.00                            | 10.44                              |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31312            | 31312                      | 0.00                                | 27.28                                  |
| 31495            | 31495                      | 0.00                                | 21.10                                  |
| 31509            | 31509                      | 0.00                                | 30.78                                  |
| 31536            | 31536                      | 0.00                                | 10.72                                  |
| 31628            | 31628                      | 0.00                                | 30.56                                  |
| 31856            | 31856                      | 0.00                                | 30.18                                  |
| 31958            | 31958                      | 0.00                                | 22.03                                  |
| 33502            | 33502                      | 0.00                                | 32.67                                  |
| 33789            | 33789                      | 0.00                                | 20.67                                  |
| 34126            | 34126                      | 0.00                                | 32.16                                  |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> Repair**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30724-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> Repair; Alfason<sup>®</sup> Repair; Linola<sup>®</sup> fat cream; Linola<sup>®</sup> H fat N

### Special notes

When selecting the *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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/substance group                                                                 | Type A | Type B | Type C |
|-------------------------------------------------------------------------------------------|--------|--------|--------|
| Linola <sup>®</sup> fat creme / Linola <sup>®</sup> H fat N / Alfason <sup>®</sup> Repair | 11     | 5      | 52     |



## Second-stage model

For differentiation of the substance/substance group *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> Repair*:

| Supplier        | Substance                     | Batch    | Sample ID | Spectra | Certificate  |
|-----------------|-------------------------------|----------|-----------|---------|--------------|
| Astellas Pharma | Alfason <sup>®</sup> Repair   | 12F18/77 | 30724     | 55      | not required |
| Astellas Pharma | Alfason <sup>®</sup> Repair   | 13E16/76 | 31069     | 40      | not required |
| Astellas Pharma | Alfason <sup>®</sup> Repair   | 16G60/75 | 32993     | 40      | not required |
| LEO Pharma GmbH | Alfason <sup>®</sup> Repair   | 17E20/75 | 33790     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 235260   | 30771     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 337280   | 31096     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 611011   | 33243     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 612211   | 33260     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> H fat N   | 333080   | 31092     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> H fat N   | 611060   | 33211     | 40      | not required |
| Dr. Wolff       | Linola <sup>®</sup> H fat N   | 801410   | 34128     | 40      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> Repair*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 11 different batches.
- 24 250 spectra from a total of 498 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<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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 <sup>®</sup> Repair   | 15K07/77 | 32562     | 40      |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 603820   | 32561     | 40      |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 607250   | 34125     | 40      |
| Dr. Wolff       | Linola <sup>®</sup> fat cream | 802990   | 34253     | 40      |
| Dr. Wolff       | Linola <sup>®</sup> H fat N   | 603230   | 32560     | 40      |
| Dr. Wolff       | Linola <sup>®</sup> H fat N   | 611060   | 33038     | 40      |

- 20 721 spectra from a total of 445 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.

- 68 spectra from 30 *Apo-Ident* customers from 52 batches from the substance/substance group *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> Repair*.
- Among them are spectra of independent samples from 52 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier  | Substance                     | Batch     | Spectra |
|-----------|-------------------------------|-----------|---------|
| Astellas  | Alfason <sup>®</sup> Repair   | 13H02/76  | 1       |
| Astellas  | Alfason <sup>®</sup> Repair   | 15J09/75  | 1       |
| GEHE      | Alfason <sup>®</sup> Repair   | 17J11/79  | 1       |
| GEHE      | Alfason <sup>®</sup> Repair   | 17J13/76  | 1       |
| GEHE      | Alfason <sup>®</sup> Repair   | 17K83/75  | 1       |
| GEHE      | Alfason <sup>®</sup> Repair   | 18EB5/75  | 1       |
| GEHE      | Alfason <sup>®</sup> Repair   | 18I90/75  | 1       |
| Phoenix   | Alfason <sup>®</sup> Repair   | 15/03/75  | 1       |
| PHoenix   | Alfason <sup>®</sup> Repair   | 17E81/75  | 2       |
| Phönix    | Alfason <sup>®</sup> Repair   | 15J09/75  | 1       |
| PHÖNIX    | Alfason <sup>®</sup> Repair   | 17E77/75  | 2       |
| PHÖNIX    | Alfason <sup>®</sup> Repair   | 17F72/75  | 1       |
| Caelo     | Linola <sup>®</sup> fat cream | 435161    | 1       |
| Caelo     | Linola <sup>®</sup> fat cream | 238540    | 1       |
| Caelo     | Linola <sup>®</sup> fat cream | 438070    | 1       |
| Caelo     | Linola <sup>®</sup> fat cream | 700320    | 1       |
| Caelo     | Linola <sup>®</sup> fat cream | 803320    | 1       |
| Dr wolff  | Linola <sup>®</sup> fat cream | 3330      | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 237920    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 333650    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 432591    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 437270    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 610320    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 705555650 | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 810180    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 101808    | 1       |
| Dr. Wolff | Linola <sup>®</sup> fat cream | 907070    | 1       |

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| Supplier                    | Substance                     | Batch       | Spectra |
|-----------------------------|-------------------------------|-------------|---------|
| Dr. Wolff                   | Linola <sup>®</sup> fat cream | 907080      | 2       |
| Dr. Wolff                   | Linola <sup>®</sup> fat cream | 909790      | 1       |
| Dr. Wolff / Alliance He...  | Linola <sup>®</sup> fat cream | 709800      | 1       |
| Dr. Wolff / Gehe            | Linola <sup>®</sup> fat cream | 337860      | 1       |
| Dr. Wolff / Anzag           | Linola <sup>®</sup> fat cream | 237710      | 1       |
| Dr. Wolff 03.12.2013Fa...   | Linola <sup>®</sup> fat cream | 337701      | 1       |
| Dr. Wolff/ Sanacorp         | Linola <sup>®</sup> fat cream | 3400        | 1       |
| Dr. Wolff/Phönix            | Linola <sup>®</sup> fat cream | 810170      | 1       |
| Dr. Wolff/Phönix            | Linola <sup>®</sup> fat cream | 700310      | 1       |
| Dr. Wolff/Phönix            | Linola <sup>®</sup> fat cream | 909790      | 1       |
| Dr. August Wolff Gmbh&Co... | Linola <sup>®</sup> fat cream | 710080      | 1       |
| Dr. August Wolff Gmbh&Co... | Linola <sup>®</sup> fat cream | 810180      | 1       |
| Dr. August Wolff Gmbh&Co... | Linola <sup>®</sup> fat cream | 909790      | 1       |
| dr.wolff                    | Linola <sup>®</sup> fat cream | 337760      | 1       |
| dr.wolff                    | Linola <sup>®</sup> fat cream | 337770      | 1       |
| dr.Wolff                    | Linola <sup>®</sup> fat cream | 438440      | 3       |
| Dr.Wolff                    | Linola <sup>®</sup> fat cream | 431160      | 1       |
| Dr.Wolff                    | Linola <sup>®</sup> fat cream | 608210      | 1       |
| Dr.Wolff                    | Linola <sup>®</sup> fat cream | 701590      | 1       |
| Dr.Wolff                    | Linola <sup>®</sup> fat cream | 810170      | 1       |
| Dr.Wolff - Noweda           | Linola <sup>®</sup> fat cream | 808280      | 1       |
| Dr.Wolff/NOW                | Linola <sup>®</sup> fat cream | 435160      | 1       |
| Dr.Wolff/Sanacorp           | Linola <sup>®</sup> fat cream | 700320      | 1       |
| Dr.Wolff/Sanacorp           | Linola <sup>®</sup> fat cream | 704020      | 1       |
| Löwen City-Apotheke Bar...  | Linola <sup>®</sup> fat cream | 231060      | 1       |
| Phönix                      | Linola <sup>®</sup> fat cream | 238540      | 1       |
| Spangro 26.02.2014          | Linola <sup>®</sup> fat cream | 337760      | 1       |
| Wolff                       | Linola <sup>®</sup> fat cream | 608200      | 1       |
| Wolff / Wolff               | Linola <sup>®</sup> fat cream | 431190      | 1       |
| Wolff/Noweda                | Linola <sup>®</sup> fat cream | 704030      | 1       |
| Wolff/Phönix                | Linola <sup>®</sup> fat cream | 710060      | 1       |
| Wolff/Phönix                | Linola <sup>®</sup> fat cream | 807620      | 1       |
| Wolff/Phönix                | Linola <sup>®</sup> fat cream | 710080      | 1       |
| Wolff/Phönix                | Linola <sup>®</sup> fat cream | 907070      | 1       |
| Wolff/Phönix                | Linola <sup>®</sup> fat cream | 337770      | 1       |
| Engel-Apotheke              | Linola <sup>®</sup> H fat N   | 2319Q-07101 | 1       |

- 9227 spectra from 772 *Apo-Ident* customers from a total of 3623 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<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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              | 24 250        |
| Type B | 0              | 238           | 2              | 20 716        |
| Type C | 0              | 61            | 7              | 9227          |

The substance/substance group *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9602 %) | 100.0000 % (> 98.6813 %) |
| <b>Type B</b> | 100.0000 % (> 99.9457 %) | 99.1667 % (> 97.9167 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7988 %) | 89.7059 % (> 85.2941 %)  |

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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.

| <b>Substance</b>                    | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|-------------------------------------|-------------------------------|---------------------------------------|
| Alfason Basis Cresa <sup>®</sup>    | 10.48                         | —                                     |
| Dermatop <sup>®</sup> base ointment | 14.92                         | —                                     |
| Excipial <sup>®</sup> lipo cream    | 29.17                         | —                                     |
| Lipolotio urea 5% F body lotion     | 53.91                         | —                                     |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Linola<sup>®</sup> fat creme / Linola<sup>®</sup> H fat N / Alfason<sup>®</sup> 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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 30724            | 30724                      | 0.00                                | 20.22                                  |
| 30771            | 30771                      | 0.00                                | 16.26                                  |
| 31069            | 31069                      | 0.00                                | 9.02                                   |
| 31092            | 31092                      | 0.00                                | 17.54                                  |
| 31096            | 31096                      | 0.00                                | 19.00                                  |
| 32993            | 32993                      | 0.00                                | 15.60                                  |
| 33211            | 33211                      | 0.00                                | 21.85                                  |

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| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 33243            | 33243                      | 0.00                                | 22.70                                  |
| 33260            | 33260                      | 0.00                                | 21.85                                  |
| 33790            | 33790                      | 0.00                                | 16.90                                  |
| 34128            | 34128                      | 0.00                                | 24.43                                  |

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 2.4-2021-02

Validated substance/substance group **Lipolotio urea 5% F body lotion**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30973-2021-06-11  
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/substance group       | 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 54 961 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.
- 24 525 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 450 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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<br>main model | Distance in<br>second-stage model |
|------------------------------------------------|---------------------------|-----------------------------------|
| Neuroderm <sup>®</sup> moisturising cream lipo | 15.84                     | —                                 |
| Dermatest base ointment                        | 16.55                     | —                                 |
| Excipial <sup>®</sup> U Lipolotio              | 34.92                     | —                                 |
| Allergika evening primrose oil cream 20%       | 36.15                     | —                                 |
| Dermifant <sup>®</sup> kids cream              | 49.54                     | —                                 |
| DMS <sup>®</sup> base cream high classic       | 64.65                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30973     | 30973                  | 0.00                            | 20.47                              |
| 31766     | 31766                  | 0.00                            | 34.52                              |
| 34362     | 34362                  | 0.00                            | 28.01                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Lygal® head ointment N 3%**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31049-2021-06-11  
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/substance group | 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<sup>®</sup> 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<sup>®</sup> head ointment N 3%*:

| Supplier | Substance                       | Batch  | Sample ID | Spectra | Certificate  |
|----------|---------------------------------|--------|-----------|---------|--------------|
| Taurus   | Lygal <sup>®</sup> head oint... | 124311 | 31049     | 40      | not required |
| Taurus   | Lygal <sup>®</sup> head oint... | 143710 | 31763     | 60      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> head ointment N 3%*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 24 605 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> head ointment N 3% | 160732 | 32763     | 40      |
| Taurus   | Lygal <sup>®</sup> head ointment N 3% | 181802 | 34127     | 40      |
| Taurus   | Lygal <sup>®</sup> head ointment N 3% | 160732 | 33261     | 40      |

- 20 841 spectra from a total of 449 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% | 184027 | 2       |
| Almirall/GEHE | Lygal® head ointment N 3% | 193815 | 1       |
| 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       |

- 9284 spectra from 772 *Apo-Ident* customers from a total of 3665 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 100           | 0              | 24 605        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 11            | 0              | 9284          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 94.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8038 %) | 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<sup>®</sup> 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<br>main model | Distance in<br>second-stage model |
|-----------------------------------------|---------------------------|-----------------------------------|
| Lygal <sup>®</sup> ointment base        | 38.77                     | —                                 |
| Stomahesive <sup>®</sup> adhesive paste | 55.08                     | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lygal<sup>®</sup> 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31049     | 31049                  | 0.00                            | 38.77                              |
| 31763     | 31763                  | 0.00                            | 38.94                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Lygal<sup>®</sup> ointment base**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31014-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Lygal<sup>®</sup> ointment base

### Special notes

When selecting the *Lygal<sup>®</sup> 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/substance group        | Type A | Type B | Type C |
|----------------------------------|--------|--------|--------|
| Lygal <sup>®</sup> ointment base | 3      | 2      | 25     |

## Second-stage model

For differentiation of the substance/substance group *Lygal<sup>®</sup> 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<sup>®</sup> ointment base*:

| Supplier | Substance                       | Batch   | Sample ID | Spectra | Certificate  |
|----------|---------------------------------|---------|-----------|---------|--------------|
| Taurus   | Lygal <sup>®</sup> ointment ... | 121302P | 31014     | 40      | not required |
| Taurus   | Lygal <sup>®</sup> ointment ... | 154841  | 32749     | 40      | not required |
| Taurus   | Lygal <sup>®</sup> ointment ... | 164201  | 32772     | 40      | not required |
| Taurus   | Lygal <sup>®</sup> ointment ... | 164201  | 33244     | 40      | not required |
| Taurus   | Lygal <sup>®</sup> ointment ... | 164201  | 33297     | 40      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> ointment base*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 505 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> ointment base | 174104  | 33988     | 40      |
| Taurus   | Lygal <sup>®</sup> ointment base | 124904P | 31704     | 60      |

- 20 861 spectra from a total of 449 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.

- 60 spectra from 27 *Apo-Ident* customers from 26 batches from the substance/substance group *Lygal<sup>®</sup> 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 <sup>®</sup> ointment base | 175007   | 4       |
| Almiral / Gehe             | Lygal <sup>®</sup> ointment base | 182905   | 2       |
| Almiral / Phönix           | Lygal <sup>®</sup> ointment base | 174106   | 1       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 175007   | 2       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 174106   | 2       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 175008   | 1       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 182002   | 1       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 182904   | 2       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 182001   | 1       |
| Almirall                   | Lygal <sup>®</sup> ointment base | 182903   | 2       |
| Almirall Hermal GmbH       | Lygal <sup>®</sup> ointment base | 192701   | 1       |
| Almirall / Gehe            | Lygal <sup>®</sup> ointment base | 175008   | 2       |
| Almirall / Gehe            | Lygal <sup>®</sup> ointment base | 174106   | 1       |
| Almirall / GEHE            | Lygal <sup>®</sup> ointment base | 182903   | 1       |
| Almirall / GE-HH           | Lygal <sup>®</sup> ointment base | 202503   | 1       |
| Almirall / Noweda          | Lygal <sup>®</sup> ointment base | 175008   | 1       |
| Almirall / Noweda          | Lygal <sup>®</sup> ointment base | 182903   | 1       |
| Almirall / Phoenix         | Lygal <sup>®</sup> ointment base | 182904   | 1       |
| Caelo                      | Lygal <sup>®</sup> ointment base | 174106   | 1       |
| Caelo                      | Lygal <sup>®</sup> ointment base | 141601P  | 1       |
| Caelo                      | Lygal <sup>®</sup> ointment base | 154841   | 1       |
| Caelo                      | Lygal <sup>®</sup> ointment base | 182903   | 1       |
| Finteler Apotheke          | Lygal <sup>®</sup> ointment base | 1704011  | 1       |
| Phoenix WE: 08.11.17 20... | Lygal <sup>®</sup> ointment base | 172803_2 | 1       |
| Sanacorp / Almirall        | Lygal <sup>®</sup> ointment base | 175008   | 1       |
| TAUROS PHARMA              | Lygal <sup>®</sup> ointment base | 124803   | 1       |
| TAUROS PHARMA              | Lygal <sup>®</sup> ointment base | 141601P  | 1       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 124803   | 2       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 133401T  | 2       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 133402   | 1       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 141601T  | 1       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 141603   | 2       |
| Taurus                     | Lygal <sup>®</sup> ointment base | 18121705 | 1       |
| Taurus / Gehe              | Lygal <sup>®</sup> ointment base | 1704011  | 1       |
| Taurus Pharma              | Lygal <sup>®</sup> ointment base | 133401T  | 2       |
| Taurus Pharma              | Lygal <sup>®</sup> ointment base | 133401P  | 1       |

*continued on the next page*



continued from previous page

| Supplier             | Substance                        | Batch    | Spectra |
|----------------------|----------------------------------|----------|---------|
| TAURUS PHARMA        | Lygal <sup>®</sup> ointment base | 141602T  | 1       |
| TAURUS PHARMA        | Lygal <sup>®</sup> ointment base | 154841   | 1       |
| Taurus Pharma / Gehe | Lygal <sup>®</sup> ointment base | 133401T  | 1       |
| Taurus Pharma GmbH   | Lygal <sup>®</sup> ointment base | 164803   | 1       |
| Taurus Pharma GmbH   | Lygal <sup>®</sup> ointment base | 172803_2 | 1       |
| Taurus/ Phönix       | Lygal <sup>®</sup> ointment base | 133401T  | 1       |
| Taurus/Alliance      | Lygal <sup>®</sup> ointment base | 1717022  | 2       |
| Taurus/Alliance      | Lygal <sup>®</sup> ointment base | 1717021  | 1       |
| Taurus/Phönix        | Lygal <sup>®</sup> ointment base | 154841   | 1       |
| TAUROS PHARMA        | Lygal <sup>®</sup> ointment base |          | 1       |

- 9235 spectra from 771 *Apo-Ident* customers from a total of 3649 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<sup>®</sup> 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<sup>®</sup> 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 100           | 0              | 20 861        |
| <b>Type C</b> | 0              | 58            | 2              | 9235          |

The substance/substance group *Lygal<sup>®</sup> 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 94.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7990 %) | 96.6667 % (> 91.6667 %)  |

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

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

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

## Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *Lygal<sup>®</sup> 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<br>main model | Distance in<br>second-stage model |
|-----------------------------------------|---------------------------|-----------------------------------|
| Lygal <sup>®</sup> head ointment N 3%   | 20.10                     | —                                 |
| Stomahesive <sup>®</sup> adhesive paste | 38.34                     | —                                 |
| Asche Basis <sup>®</sup> fat ointment   | 107.67                    | —                                 |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Lygal<sup>®</sup> 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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31014     | 31014                  | 0.00                            | 21.72                              |
| 32749     | 32749                  | 0.00                            | 26.01                              |
| 32772     | 32772                  | 0.00                            | 31.51                              |
| 33244     | 33244                  | 0.00                            | 27.95                              |
| 33297     | 33297                  | 0.00                            | 23.65                              |

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 2.4-2021-02

Validated substance/substance group **Mandarin oil, green**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33798-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------------|---------------------------|-----------------------------------|
| Citric oil              | 25.30                     | —                                 |
| Lime oil                | 29.22                     | —                                 |
| Grapefruit oil, organic | 36.43                     | —                                 |
| Orange oil              | 50.09                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33798     | 33798                  | 0.00                            | 24.83                              |
| 33806     | 33806                  | 0.00                            | 25.23                              |

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 2.4-2021-02

Validated substance/substance group **Manuka oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31545-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 841 spectra from a total of 449 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 | 23694-122415 | 1       |
| Taoasis           | Manuka oil | 42798-125299 | 3       |
| Taoasis           | Manuka oil | 65261-127051 | 1       |
| Taoasis           | Manuka oil | 42798-126332 | 2       |
| 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       |

- 9276 spectra from 772 *Apo-Ident* customers from a total of 3664 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 19            | 0              | 9276          |

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 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| Type B | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| Type C | 100.0000 % (> 98.8013 %) | 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 | 13.13                  | —                              |
| Myrtle oil          | 35.80                  | —                              |
| Immortelle oil      | 37.85                  | —                              |
| Citrus oil          | 39.75                  | —                              |
| Cardamom oil        | 47.33                  | —                              |
| Hyssop oil          | 47.51                  | —                              |
| Marjoram oil        | 47.64                  | —                              |
| Cumin oil           | 49.48                  | —                              |
| Cedar wood oil      | 54.22                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31545     | 31545               | 0.00                         | 34.50                           |
| 31655     | 31655               | 0.00                         | 33.75                           |
| 33994     | 33994               | 0.00                         | 25.53                           |
| 35075     | 35075               | 0.00                         | 22.36                           |

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Marjoram oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30454-2021-06-11  
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/substance group | 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 54 961 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.
- 24 485 spectra from a total of 504 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 449 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       |

- 9262 spectra from 772 *Apo-Ident* customers from a total of 3655 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              | 24 485        |
| Type B | 0              | 80            | 0              | 20 881        |
| Type C | 0              | 32            | 1              | 9262          |

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 % (> 99.9603 %) | 100.0000 % (> 97.2727 %) |
| Type B | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| Type C | 100.0000 % (> 98.7999 %) | 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 | 22.85                  | –                              |
| Tea tree oil    | 26.43                  | –                              |
| Cypress oil     | 63.63                  | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31137     | 31137               | 0.00                         | 66.38                           |
| 32067     | 32067               | 0.00                         | 41.60                           |

*continued on the next page*



*continued from previous page*

| <b>Sample ID</b> | <b>Reference<br/>sample ID</b> | <b>Distance to<br/>reference sample</b> | <b>Distance to<br/>next foreign sample</b> |
|------------------|--------------------------------|-----------------------------------------|--------------------------------------------|
| 32819            | 32819                          | 0.00                                    | 52.46                                      |
| 34275            | 34275                          | 0.00                                    | 67.98                                      |
| 34436            | 34436                          | 0.00                                    | 45.24                                      |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Matricaria oil, morrocan</b>                                 |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30844-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 2022-960    | 1       |
| Taoasis/Taoasis | Matricaria oil, morrocan | 1814-127407 | 1       |
| Taoasis/Taoasis | Matricaria oil, morrocan | 5081-8452   | 1       |

- 9290 spectra from 772 *Apo-Ident* customers from a total of 3670 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 109           | 11             | 20 841        |
| <b>Type C</b> | 0              | 3             | 2              | 9290          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 90.8333 % (> 88.3333 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8109 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------|---------------------------|-----------------------------------|
| Thyme oil, white  | 28.73                     | —                                 |
| Citrus oil        | 40.50                     | —                                 |
| Marjoram oil      | 43.14                     | —                                 |
| Angelica root oil | 45.52                     | —                                 |
| Carrot seed oil   | 53.01                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31579     | 31579                  | 0.00                            | 37.48                              |
| 31841     | 31841                  | 0.00                            | 39.52                              |
| 32269     | 32269                  | 0.00                            | 48.98                              |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Matricaria oil, roman**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31254-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 450 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 | 1850119-119451 | 1       |
| Taoasis  | Matricaria oil, roman | 1511-122183    | 1       |
| Taoasis  | Matricaria oil, roman | 1850119-121467 | 1       |
| Taoasis  | Matricaria oil, roman | 1638-123706    | 1       |
| Taoasis  | Matricaria oil, roman | 8941-125875    | 1       |
| Taoasis  | Matricaria oil, roman | 1930-126600    | 7       |
| Taoasis  | Matricaria oil, roman | 2033-3091      | 5       |

- 9276 spectra from 772 *Apo-Ident* customers from a total of 3666 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 66            | 14             | 20 881        |
| <b>Type C</b> | 0              | 19            | 0              | 9276          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 82.5000 % (> 78.7500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8013 %) | 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<br>main model | Distance in<br>second-stage model |
|----------------------|---------------------------|-----------------------------------|
| Hyssop oil           | 33.99                     | —                                 |
| Sage oil             | 36.46                     | —                                 |
| Rosemary camphor oil | 50.01                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31254     | 31254                  | 0.00                            | 36.28                              |
| 31686     | 31686                  | 0.00                            | 37.48                              |
| 33989     | 33989                  | 0.00                            | 33.99                              |

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 2.4-2021-02

Validated substance/substance group **Melissa oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33800-2021-06-11  
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/substance group | 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 54 961 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.
- 24 555 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 150           | 0              | 24 555        |
| <b>Type B</b> | 0              | 0             | 40             | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 96.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 0.0000 % (≥ 0.0000 %)    |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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      | 15.28                  | —                              |
| Ginger oil          | 23.16                  | —                              |
| Lemon grass oil     | 32.14                  | —                              |
| Cedar wood oil      | 33.34                  | —                              |
| Spearmint oil       | 35.04                  | —                              |
| Swiss pine oil      | 36.29                  | —                              |
| Citrus oil          | 37.00                  | —                              |
| Cypress oil         | 39.38                  | —                              |
| Myrtle oil          | 40.39                  | —                              |
| Citronella oil      | 44.10                  | —                              |
| Vetiver bourbon oil | 47.86                  | —                              |
| Marjoram oil        | 48.23                  | —                              |
| Lime oil            | 50.16                  | —                              |

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                         | 20.53                           |
| 33831     | 33831               | 0.00                         | 20.50                           |
| 34298     | 34298               | 0.00                         | 17.85                           |
| 34404     | 34404               | 0.00                         | 17.23                           |

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 2.4-2021-02

Validated substance/substance group **Melissa oil 30%**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33812-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 931 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 30            | 0              | 20 931        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9462 %) | 100.0000 % (> 80.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|--------------------------|---------------------------|-----------------------------------|
| Petitgrain oil           | 27.31                     | —                                 |
| Neroli oil               | 31.18                     | —                                 |
| Thyme oil, white         | 37.74                     | —                                 |
| Lavender oil             | 40.15                     | —                                 |
| Coriander oil            | 43.62                     | —                                 |
| Spearmint oil            | 46.61                     | —                                 |
| Juniper oil              | 47.61                     | —                                 |
| Matricaria oil, morrocan | 50.48                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33812     | 33812                  | 0.00                            | 27.31                              |
| 33962     | 33962                  | 0.00                            | 30.65                              |

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 2.4-2021-02

Validated substance/substance group **Myrrh oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30748-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 449 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       |

- 9290 spectra from 772 *Apo-Ident* customers from a total of 3671 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 79            | 41             | 20 841        |
| <b>Type C</b> | 0              | 4             | 1              | 9290          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 65.8333 % (> 63.3333 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8109 %) | 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              | 49.58                  | –                              |
| Grapefruit oil, organic | 52.81                  | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31692     | 31692               | 0.00                         | 111.48                          |
| 32271     | 32271               | 0.00                         | 154.57                          |
| 33992     | 33992               | 0.00                         | 44.41                           |

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 2.4-2021-02

Validated substance/substance group **Neroli oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31260-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 841 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 40            | 80             | 20 841        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 33.3333 % (> 30.8333 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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            | 32.24                  | —                              |
| Thyme oil, white         | 38.27                  | —                              |
| Lavender oil             | 42.64                  | —                              |
| Matricaria oil, morrocan | 46.69                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31260     | 31260               | 0.00                         | 47.05                           |
| 31695     | 31695               | 0.00                         | 50.95                           |
| 34283     | 34283               | 0.00                         | 53.80                           |
| 34406     | 34406               | 0.00                         | 42.64                           |

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 2.4-2021-02

Validated substance/substance group **Neuroderm® moisturising cream lipo**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30721-2021-06-11  
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/substance group          | Type A | Type B | Type C |
|------------------------------------|--------|--------|--------|
| Neuroderm® moisturising cream lipo | 3      | 2      | 1      |

## Second-stage model

For differentiation of the substance/substance group *Neuroderm<sup>®</sup> 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<sup>®</sup> moisturising cream lipo*:

| Supplier     | Substance                       | Batch     | Sample ID | Spectra | Certificate  |
|--------------|---------------------------------|-----------|-----------|---------|--------------|
| Infectopharm | Neuroderm <sup>®</sup> moist... | S031202.1 | 30721     | 40      | not required |
| Infectopharm | Neuroderm <sup>®</sup> moist... | S031506.1 | 31672     | 60      | not required |
| Infectopharm | Neuroderm <sup>®</sup> moist... | S051723.1 | 34045     | 40      | not required |

## Validation samples

A total of 54 961 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<sup>®</sup> moisturising cream lipo*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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<sup>®</sup> 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 <sup>®</sup> moisturising crea... | S071617.2 | 32739     | 40      |
| Infectopharm | Neuroderm <sup>®</sup> moisturising crea... | S021706.1 | 33287     | 40      |

- 20 881 spectra from a total of 449 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       |

- 9293 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 2             | 0              | 9293          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8304 %) | 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                  | 24.49                  | —                              |
| Lipolotio urea 5% F body lotion          | 24.54                  | —                              |
| Allergika evening primrose oil cream 20% | 53.28                  | —                              |

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                         | 30.85                           |
| 31672     | 31672               | 0.00                         | 24.36                           |
| 34045     | 34045               | 0.00                         | 30.55                           |

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 2.4-2021-02

Validated substance/substance group **Nicotine**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31019-2021-06-11  
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/substance group | 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 54 961 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.
- 24 520 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 185           | 0              | 24 520        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.7568 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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 | 153.42                 | –                              |

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                         | 169.82                          |
| 31508     | 31508               | 0.00                         | 168.50                          |
| 31518     | 31518               | 0.00                         | 168.80                          |
| 31948     | 31948               | 0.00                         | 169.40                          |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | Ointment ash basis / Neribas <sup>®</sup>                       |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30774-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany |

### Relevant substance names

Ointment ash basis / Neribas<sup>®</sup>; Asche Basis<sup>®</sup> ointment; Neribas<sup>®</sup> ointment

### Special notes

When selecting the *Ointment ash basis / Neribas<sup>®</sup>* 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/substance group                 | Type A | Type B | Type C |
|-------------------------------------------|--------|--------|--------|
| Ointment ash basis / Neribas <sup>®</sup> | 3      | 4      | 109    |

## Second-stage model

For differentiation of the substance/substance group *Ointment ash basis* / *Neribas*<sup>®</sup> the following second-stage model is used:

*no second-stage model*

## Calibration samples

Only spectra which have been recorded by *HiperScan 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*<sup>®</sup>:

| Supplier  | Substance                         | Batch  | Sample ID | Spectra | Certificate  |
|-----------|-----------------------------------|--------|-----------|---------|--------------|
| Chiesi    | Asche Basis <sup>®</sup> oin. ... | 21038A | 30774     | 40      | not required |
| Chiesi    | Asche Basis <sup>®</sup> oin. ... | 21038A | 30833     | 40      | not required |
| Chiesi    | Asche Basis <sup>®</sup> oin. ... | 21038A | 31080     | 40      | not required |
| Bayer     | Neribas <sup>®</sup> ointment     | 21053B | 30969     | 40      | not required |
| Bayer     | Neribas <sup>®</sup> ointment     | 21053B | 30994     | 40      | not required |
| Jenapharm | Neribas <sup>®</sup> ointment     | 31064C | 31093     | 40      | not required |

## Validation samples

A total of 54 961 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*<sup>®</sup>. These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 465 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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*<sup>®</sup>.
- 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 <sup>®</sup> ointment | 61067A  | 32590     | 40      |
| Chiesi    | Asche Basis <sup>®</sup> ointment | 17072A  | 33840     | 40      |
| Jenapharm | Neribas <sup>®</sup> ointment     | YY00TJ0 | 32564     | 40      |
| Jenapharm | Neribas <sup>®</sup> ointment     | YY016EC | 33288     | 40      |
| Chiesi    | Asche Basis <sup>®</sup> ointment | 61067A  | 32924     | 40      |
| Chiesi    | Asche Basis <sup>®</sup> ointment | 61067A  | 32927     | 40      |

- 20 721 spectra from a total of 447 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.

- 277 spectra from 66 *Apo-Ident* customers from 109 batches from the substance/substance group *Ointment ash basis / Neribas<sup>®</sup>*.
- Among them are spectra of independent samples from 108 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier                     | Substance                         | Batch  | Spectra |
|------------------------------|-----------------------------------|--------|---------|
| Alliance Healthcare          | Asche Basis <sup>®</sup> ointment | 92083A | 1       |
| Anzag/Ichtyol-Gesellsch. ... | Asche Basis <sup>®</sup> ointment | 23043A | 1       |
| Caelo                        | Asche Basis <sup>®</sup> ointment | 31047A | 1       |
| Caelo                        | Asche Basis <sup>®</sup> ointment | 81708A | 1       |
| Caelo                        | Asche Basis <sup>®</sup> ointment | 83079A | 2       |
| Chiese                       | Asche Basis <sup>®</sup> ointment | 63069A | 1       |
| Chiese                       | Asche Basis <sup>®</sup> ointment | 63070A | 1       |
| Chiese                       | Asche Basis <sup>®</sup> ointment | 71073A | 2       |
| Chiese/Sanacorp WE:07.0...   | Asche Basis <sup>®</sup> ointment | 52062A | 1       |
| chiesi                       | Asche Basis <sup>®</sup> ointment | 42055A | 1       |
| chiesi                       | Asche Basis <sup>®</sup> ointment | 44057A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 32048A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 33049A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 34051A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 41052A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 41054A | 3       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 51060A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 51060A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 52062A | 3       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 52063A | 3       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 53065A | 2       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 63069A | 3       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 63068A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 83079A | 1       |
| Chiesi                       | Asche Basis <sup>®</sup> ointment | 83080A | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> ointment | 33049A | 1       |
| Chiesi / Gehe                | Asche Basis <sup>®</sup> ointment | 33050A | 1       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> ointment | 2088A  | 3       |
| Chiesi / Noweda              | Asche Basis <sup>®</sup> ointment | 3090A  | 1       |
| Chiesi / Phönix              | Asche Basis <sup>®</sup> ointment | 83079A | 1       |
| Chiesi / Phönix              | Asche Basis <sup>®</sup> ointment | 91082A | 3       |
| Chiesi / Phönix              | Asche Basis <sup>®</sup> ointment | 92084A | 2       |

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| Supplier               | Substance                         | Batch      | Spectra |
|------------------------|-----------------------------------|------------|---------|
| Chiesi / Phönix        | Asche Basis <sup>®</sup> ointment | 83080A     | 1       |
| Chiesi / Phönix        | Asche Basis <sup>®</sup> ointment | 92086A     | 1       |
| Chiesi / Phönix        | Asche Basis <sup>®</sup> ointment | 92083A     | 1       |
| Chiesi / Phönix        | Asche Basis <sup>®</sup> ointment | 92087A     | 1       |
| Chiesi / Phönix        | Asche Basis <sup>®</sup> ointment | 94087A     | 1       |
| Chiesi / Sanacorp      | Asche Basis <sup>®</sup> ointment | 92084A     | 1       |
| Chiesi / Sanacorp      | Asche Basis <sup>®</sup> ointment | 92086A     | 1       |
| chiesi / Gehe          | Asche Basis <sup>®</sup> ointment | 73075A     | 1       |
| Chiesi / Jenne         | Asche Basis <sup>®</sup> ointment | 92437A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 21039A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 52062A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 52064A     | 3       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 53065A     | 4       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 61066A     | 2       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 63070A     | 2       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 71071A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 71073A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 71072A     | 1       |
| Chiesi GmbH            | Asche Basis <sup>®</sup> ointment | 72074A     | 1       |
| Chiesi GmbH / Sanacorp | Asche Basis <sup>®</sup> ointment | 92034A     | 1       |
| Chiesi GmbH/Phoenix    | Asche Basis <sup>®</sup> ointment | 91082A     | 1       |
| Chiesi GmbH/Phoenix    | Asche Basis <sup>®</sup> ointment | 92083A     | 3       |
| Chiesi/ Anzag          | Asche Basis <sup>®</sup> ointment | 83079A     | 1       |
| CHIESI/ NOWEDA         | Asche Basis <sup>®</sup> ointment | 51060A     | 2       |
| Chiesi/ sanacorp       | Asche Basis <sup>®</sup> ointment | 92086A     | 1       |
| Chiesi/ Sanacorp       | Asche Basis <sup>®</sup> ointment | 92085A     | 1       |
| Chiesi/AHD             | Asche Basis <sup>®</sup> ointment | 31045A     | 4       |
| Chiesi/AHD             | Asche Basis <sup>®</sup> ointment | 31047A     | 1       |
| Chiesi/AHD             | Asche Basis <sup>®</sup> ointment | 33049A     | 1       |
| Chiesi/Alliance        | Asche Basis <sup>®</sup> ointment | 61067A     | 1       |
| Chiesi/Anzag           | Asche Basis <sup>®</sup> ointment | 1 (92084A) | 1       |
| chiesi/gehe            | Asche Basis <sup>®</sup> ointment | 71072A     | 1       |
| Chiesi/Gehe            | Asche Basis <sup>®</sup> ointment | 42056A     | 1       |
| Chiesi/Gehe            | Asche Basis <sup>®</sup> ointment | 83079A     | 1       |
| Chiesi/Gehe            | Asche Basis <sup>®</sup> ointment | 92085A     | 1       |
| Chiesi/Gehe            | Asche Basis <sup>®</sup> ointment | 2088A      | 1       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 73076A     | 1       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 74077A     | 2       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 91082A     | 2       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 92084A     | 1       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 925084A    | 1       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 92086A     | 2       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 92083A     | 5       |
| Chiesi/Jenne           | Asche Basis <sup>®</sup> ointment | 2001A      | 1       |
| Chiesi/Krieger         | Asche Basis <sup>®</sup> ointment | 61066A     | 1       |
| Chiesi/Noweda          | Asche Basis <sup>®</sup> ointment | 71072A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 23042A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 73076A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 73075A     | 3       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 74077A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 83079A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 84081A     | 3       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 91082A     | 2       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 92084A     | 3       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 92086A     | 2       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 94087A     | 1       |
| Chiesi/Phoenix         | Asche Basis <sup>®</sup> ointment | 2089A      | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> ointment | 51059A     | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> ointment | 71073A     | 1       |
| Chiesi/Phönix          | Asche Basis <sup>®</sup> ointment | 72074A     | 2       |

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| Supplier                   | Substance                         | Batch       | Spectra |
|----------------------------|-----------------------------------|-------------|---------|
| Chiesi/Phönix              | Asche Basis <sup>®</sup> ointment | 81078A      | 1       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> ointment | 84081A      | 2       |
| Chiesi/Phönix              | Asche Basis <sup>®</sup> ointment | 3090A       | 2       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> ointment | 41053A      | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> ointment | 71072A      | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> ointment | 83080A      | 1       |
| Chiesi/Sanacorp            | Asche Basis <sup>®</sup> ointment | 92084A      | 1       |
| Chiesi                     | Asche Basis <sup>®</sup> ointment | 52063A      | 2       |
| Gehe                       | Asche Basis <sup>®</sup> ointment | 17I21-B01   | 1       |
| Caelo                      | Asche Basis <sup>®</sup> ointment | 63068A      | 3       |
| Caelo                      | Asche Basis <sup>®</sup> ointment | 61067A      | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 71072A      | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 84081A      | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 83080A      | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 92085A      | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 2088A       | 1       |
| Noweda                     | Asche Basis <sup>®</sup> ointment | 2089A       | 2       |
| Phoenix/Chiesi             | Asche Basis <sup>®</sup> ointment | 2088A       | 2       |
| Phönix                     | Asche Basis <sup>®</sup> ointment | 31047A      | 1       |
| Phönix/ Chiesi             | Asche Basis <sup>®</sup> ointment | 92083A      | 1       |
| Phönix/ Chiesi             | Asche Basis <sup>®</sup> ointment | 83080A      | 1       |
| PPL                        | Asche Basis <sup>®</sup> ointment | 61067A      | 1       |
| PPL                        | Asche Basis <sup>®</sup> ointment | 71072A      | 2       |
| PPL                        | Asche Basis <sup>®</sup> ointment | 73075A      | 1       |
| Sanacorp WE 29.04.17 -8... | Asche Basis <sup>®</sup> ointment | 63070A      | 1       |
| Sanacorp/Chiesi WE:31.0... | Asche Basis <sup>®</sup> ointment | 41054A      | 1       |
| SanacorpWE:9.12.2016 ...   | Asche Basis <sup>®</sup> ointment | 63068A      | 1       |
| WE:27.02.2016 Sanacor...   | Asche Basis <sup>®</sup> ointment | 52063A      | 1       |
| WE:Sanacorp19.01.2016 ...  | Asche Basis <sup>®</sup> ointment | 52064A      | 2       |
| WE14.12.16 Chiesi/Sanac... | Asche Basis <sup>®</sup> ointment | 61067A      | 2       |
| Wolff/AHD                  | Asche Basis <sup>®</sup> ointment | 32048A      | 2       |
| Audor Pharma               | Neribas <sup>®</sup> ointment     | YY02825     | 1       |
| Bayer                      | Neribas <sup>®</sup> ointment     | YY01KHH     | 1       |
| Bayer/ Sanacorp            | Neribas <sup>®</sup> ointment     | YY006JT     | 3       |
| Bayer/Sanacorp             | Neribas <sup>®</sup> ointment     | YY00THL     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY016EC     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY00TJ0     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY00XEH     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY016LN     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY00CC8     | 1       |
| Caelo                      | Neribas <sup>®</sup> ointment     | YY00THL     | 2       |
| Gehe                       | Neribas <sup>®</sup> ointment     | YY023JE     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | 12091812    | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY006JT     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY00XEH     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY016LN     | 2       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY00TJ0     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY016EC     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY017LF     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY01FX4     | 3       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY01KHH     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY01TF3     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | 5121811     | 1       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY02825     | 4       |
| Jenapharm                  | Neribas <sup>®</sup> ointment     | YY02L88     | 2       |
| Jenapharm / Anzag          | Neribas <sup>®</sup> ointment     | YY00THL     | 1       |
| Jenapharm / Anzag          | Neribas <sup>®</sup> ointment     | 75(YY02825) | 1       |
| Jenapharm / Anzag          | Neribas <sup>®</sup> ointment     | 76(YY02825) | 1       |
| Jenapharm / Anzag          | Neribas <sup>®</sup> ointment     | 80(YY02L27) | 1       |
| Jenapharm / Anzag          | Neribas <sup>®</sup> ointment     | 84(YY02L88) | 1       |

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| Supplier                   | Substance                         | Batch        | Spectra |
|----------------------------|-----------------------------------|--------------|---------|
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 70 (YY01YEX) | 1       |
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 71 (YY023J1) | 1       |
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 72 (YY02835) | 1       |
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 81 (YY02L27) | 1       |
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 82 (YY02L88) | 1       |
| Jenapharm Anzag            | Neribas <sup>®</sup> ointment     | 83 (YY02L88) | 1       |
| Jenapharm GmbH             | Neribas <sup>®</sup> ointment     | YY019PE      | 1       |
| Jenapharm/ Anzag           | Neribas <sup>®</sup> ointment     | YY00K7E      | 2       |
| Jenapharm/ Anzag           | Neribas <sup>®</sup> ointment     | 77 (YY02825) | 1       |
| Jenapharm/ Anzag           | Neribas <sup>®</sup> ointment     | 78 (YY02L27) | 1       |
| Jenapharm/ Anzag           | Neribas <sup>®</sup> ointment     | 79 (YY02L27) | 1       |
| Jenapharm/ Gehe            | Neribas <sup>®</sup> ointment     | YY023J1      | 1       |
| Jenapharm/ Gehe            | Neribas <sup>®</sup> ointment     | YY02825      | 3       |
| Jenapharm/ Gehe            | Neribas <sup>®</sup> ointment     | YY02L27      | 2       |
| Jenapharm/ Gehe            | Neribas <sup>®</sup> ointment     | YY02L88      | 1       |
| Jenapharm/ Sanacorp        | Neribas <sup>®</sup> ointment     | YY00THL      | 1       |
| Jenapharm/ Sanacorp        | Neribas <sup>®</sup> ointment     | YY01TF3      | 2       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 58 (YY0180C) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 59 (YY01KHH) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 58 (YY01FX4) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 61 (YY01KHH) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 60 (YY01KHH) | 2       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 62 (YY01KHH) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 65 (YY019PE) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 66 (YY01TF3) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 67 (YY01TF3) | 1       |
| Jenapharm/AHD              | Neribas <sup>®</sup> ointment     | 68 (YY01YEX) | 1       |
| Jenapharm/Alliance         | Neribas <sup>®</sup> ointment     | YY016EC      | 1       |
| Jenapharm/Anzag            | Neribas <sup>®</sup> ointment     | YY00XEH      | 2       |
| Jenapharm/Anzag            | Neribas <sup>®</sup> ointment     | 69 (YY01YEX) | 1       |
| Jenapharm/Gehe             | Neribas <sup>®</sup> ointment     | YY01FX4      | 1       |
| Jenapharm/Gehe             | Neribas <sup>®</sup> ointment     | YY01YEX      | 1       |
| Jenapharm/Gehe             | Neribas <sup>®</sup> ointment     | YY023JE      | 1       |
| Jenapharm/Gehe             | Neribas <sup>®</sup> ointment     | YY02L88      | 1       |
| Jenapharm/Jenne            | Neribas <sup>®</sup> ointment     | 61 (YY019PE) | 1       |
| Jenapharm/Jenne            | Neribas <sup>®</sup> ointment     | YY01TF3      | 1       |
| Jenapharm/Noweda           | Neribas <sup>®</sup> ointment     | YY00THL      | 1       |
| Jenapharm/Phoenix          | Neribas <sup>®</sup> ointment     | YY023JE      | 1       |
| Jenapharm/Phönix           | Neribas <sup>®</sup> ointment     | YY006JT      | 1       |
| Jenapharm/Phönix           | Neribas <sup>®</sup> ointment     | YY01KHH      | 1       |
| Jenapharm/Sanacorp         | Neribas <sup>®</sup> ointment     | YY0180C      | 1       |
| Karo Pharma AB/ Noweda/... | Neribas <sup>®</sup> ointment     | YY04F1P      | 1       |
| Leo Pharma / Phönix        | Neribas <sup>®</sup> ointment     | YY0431X      | 1       |
| LeoPharm/Alliance          | Neribas <sup>®</sup> ointment     | YY01FX4      | 1       |
| Leopharma/Jenne            | Neribas <sup>®</sup> ointment     | YY02L88      | 3       |
| Phönix                     | Neribas <sup>®</sup> ointment     | YY0431Y      | 1       |
| Römer/apo                  | Neribas <sup>®</sup> ointment     | YY008RJ      | 1       |
| Wolf Apotheke              | Neribas <sup>®</sup> ointment     | 73 (YY02825) | 1       |
| Wolf Apotheke              | Neribas <sup>®</sup> ointment     | 74 (YY02825) | 1       |
| Chiesi/Jenne               | Asche Basis <sup>®</sup> ointment |              | 1       |

- 9018 spectra from 771 *Apo-Ident* customers from a total of 3567 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 24 465        |
| <b>Type B</b> | 0              | 240           | 0              | 20 641        |
| <b>Type C</b> | 0              | 258           | 19             | 9018          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9603 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9453 %) | 100.0000 % (> 97.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7981 %) | 93.1408 % (> 92.0578 %)  |

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

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

Where the number of spectra does 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 | 24.04                  | –                              |
| Alfason Basis Cresa®           | 25.85                  | –                              |
| Linola® fat cream              | 56.56                  | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30774     | 30774               | 0.00                         | 34.06                           |
| 30833     | 30833               | 0.00                         | 35.89                           |
| 30969     | 30969               | 0.00                         | 38.34                           |
| 30994     | 30994               | 0.00                         | 34.85                           |
| 31080     | 31080               | 0.00                         | 33.41                           |
| 31093     | 31093               | 0.00                         | 30.83                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Orange aroma**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31190-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Orange aroma              | 6      | 6      | 59     |

## 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*    |
| Caelo    | Orange aroma | 20000419         | 35255     | 40      | 20200220*    |
| 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 54 961 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 260 spectra of 6 reference samples from the substance/substance group *Orange aroma*. These samples are listed above in the [calibration samples](#) section. The reference samples come from 6 different batches.
- 24 445 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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*.

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

- Among them are spectra of independent samples from 6 batches from which no spectra have been included in the database structure. They are sorted upwards in the following table and separated from the additional samples by a line.

| Supplier | Substance    | Batch  | Sample ID | Spectra |
|----------|--------------|--------|-----------|---------|
| Caelo    | 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      |

- 20 721 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.

- 267 spectra from 147 *Apo-Ident* customers from 61 batches from the substance/substance group *Orange aroma*.
- Among them are spectra of independent samples from 59 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier       | Substance    | Batch        | Spectra |
|----------------|--------------|--------------|---------|
| Allergika/Kehr | Orange aroma | 16056107     | 1       |
| Audor Pharma   | Orange aroma | 15215409     | 1       |
| Caelo          | Orange aroma | 12216712     | 2       |
| Caelo          | Orange aroma | 23051201     | 1       |
| 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 | 15215408     | 4       |
| Caelo          | Orange aroma | 15215410     | 1       |
| Caelo          | Orange aroma | 16056105     | 9       |
| Caelo          | Orange aroma | 16206301     | 3       |
| Caelo          | Orange aroma | 16347005     | 10      |
| Caelo          | Orange aroma | 16056108     | 1       |
| Caelo          | Orange aroma | 17055104     | 1       |
| Caelo          | Orange aroma | 17055103     | 2       |
| Caelo          | Orange aroma | 17055110     | 1       |
| Caelo          | Orange aroma | 17300509     | 7       |
| Caelo          | Orange aroma | 18205701     | 12      |
| Caelo          | Orange aroma | 19093301     | 9       |
| Caelo          | Orange aroma | 19093312     | 2       |
| Caelo          | Orange aroma | 19093311     | 7       |
| Caelo          | Orange aroma | 92968005     | 1       |
| Caelo          | Orange aroma | 192968005    | 1       |
| Caelo          | Orange aroma | 14150706     | 4       |
| Caelo          | Orange aroma | 17300507     | 10      |
| Caelo          | Orange aroma | 19093307     | 4       |
| Caelo          | Orange aroma | 200000419003 | 1       |
| Caelo          | Orange aroma | 19093302     | 1       |

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| Supplier                   | Substance    | Batch            | Spectra |
|----------------------------|--------------|------------------|---------|
| Caelo                      | Orange aroma | 18083103         | 9       |
| Caelo                      | Orange aroma | 14150714         | 2       |
| Caelo                      | Orange aroma | 20000419006      | 6       |
| Caelo                      | Orange aroma | 13123305         | 2       |
| Caelo                      | Orange aroma | 18205702         | 1       |
| Caelo                      | Orange aroma | 19093309         | 1       |
| Caelo                      | Orange aroma | 14352903         | 1       |
| Caelo                      | Orange aroma | 18326113         | 7       |
| Caelo                      | Orange aroma | 16347012         | 2       |
| Caelo                      | Orange aroma | 15215401         | 2       |
| Caelo                      | Orange aroma | 20000419003      | 2       |
| Caelo                      | Orange aroma | 192968003        | 10      |
| Caelo                      | Orange aroma | 17300501         | 9       |
| Caelo                      | Orange aroma | 12356502         | 1       |
| Caelo                      | Orange aroma | 20003349005      | 1       |
| Caelo                      | Orange aroma | 13406101         | 2       |
| Caelo                      | Orange aroma | 14352904         | 3       |
| Caelo                      | Orange aroma | 160566107        | 1       |
| Caelo                      | Orange aroma | 18326108         | 5       |
| Caelo                      | Orange aroma | 14352906         | 2       |
| Caelo                      | Orange aroma | 16056107         | 5       |
| Caesar & Loretz GmbH       | Orange aroma | 18205701         | 2       |
| 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         | 2       |
| Caesar & Loretz GmbH       | Orange aroma | 19093311         | 4       |
| 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      | 2       |
| 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       |
| Gehe amax                  | Orange aroma | 192968003        | 1       |
| 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       |

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| Supplier | Substance    | Batch | Spectra |
|----------|--------------|-------|---------|
| Caelo    | Orange aroma |       | 1       |

- 9028 spectra from 759 *Apo-Ident* customers from a total of 3614 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              | 260           | 0              | 24 445        |
| Type B | 0              | 240           | 0              | 20 721        |
| Type C | 0              | 265           | 2              | 9028          |

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 % (> 99.9603 %) | 100.0000 % (> 97.6923 %) |
| Type B | 100.0000 % (> 99.9453 %) | 100.0000 % (> 97.5000 %) |
| Type C | 100.0000 % (> 98.7981 %) | 99.2509 % (> 98.1273 %)  |

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

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

Where the number of spectra does 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 | 35.62                  | —                              |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the sub-



stance/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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31190     | 31190               | 0.00                         | 60.07                           |
| 31402     | 31402               | 0.00                         | 60.30                           |
| 31510     | 31510               | 0.00                         | 106.20                          |
| 33100     | 33100               | 0.00                         | 62.50                           |
| 35087     | 35087               | 0.00                         | 101.05                          |
| 35255     | 35255               | 0.00                         | 52.71                           |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Oregano oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31554-2021-06-11  
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/substance group | 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 54 961 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.
- 24 465 spectra from a total of 504 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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       |

- 9294 spectra from 772 *Apo-Ident* customers from a total of 3674 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 240           | 0              | 24 465        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 1             | 0              | 9294          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9603 %) | 100.0000 % (> 97.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8630 %) | 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 | 32.70                  | —                              |
| Savory herb    | 65.47                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31554     | 31554               | 0.00                         | 94.88                           |
| 31779     | 31779               | 0.00                         | 137.86                          |
| 32769     | 32769               | 0.00                         | 48.21                           |
| 33649     | 33649               | 0.00                         | 51.02                           |
| 34368     | 34368               | 0.00                         | 68.07                           |

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 2.4-2021-02

Validated substance/substance group **Palmarosa oil, organic**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30597-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

*continued on the next page*



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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      |

- 20 761 spectra from a total of 447 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       |

- 9288 spectra from 772 *Apo-Ident* customers from a total of 3670 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 200           | 0              | 20 761        |
| <b>Type C</b> | 0              | 7             | 0              | 9288          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 97.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8072 %) | 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.

| <b>Substance</b> | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|------------------|-------------------------------|---------------------------------------|
| Marjoram oil     | 95.91                         | –                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31828            | 31828                      | 0.00                                | 121.96                                 |
| 33043            | 33043                      | 0.00                                | 106.37                                 |
| 34289            | 34289                      | 0.00                                | 114.55                                 |

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 2.4-2021-02

Validated substance/substance group **Panthenol ointment Lichtenstein**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30727-2021-06-11  
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/substance group       | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------------------------------|---------------------------|-----------------------------------|
| La Roche-Posay Cold Cream Naturel | 99.41                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30727     | 30727                  | 0.00                            | 187.25                             |
| 31091     | 31091                  | 0.00                            | 184.33                             |
| 31764     | 31764                  | 0.00                            | 155.74                             |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Patchouli oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31547-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 801 spectra from a total of 448 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       |

- 9293 spectra from 772 *Apo-Ident* customers from a total of 3673 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 73            | 87             | 20 801        |
| <b>Type C</b> | 0              | 1             | 1              | 9293          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 45.6250 % (> 43.7500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8304 %) | 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 | 23.69                  | —                              |
| Marjoram oil    | 25.66                  | —                              |
| Carrot seed oil | 29.45                  | —                              |
| Tea tree oil    | 29.60                  | —                              |
| Cedar wood oil  | 32.62                  | —                              |
| Immortelle oil  | 45.11                  | —                              |
| Cypress oil     | 50.26                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31547     | 31547               | 0.00                         | 23.69                           |
| 31619     | 31619               | 0.00                         | 36.00                           |
| 32172     | 32172               | 0.00                         | 36.05                           |

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 2.4-2021-02

Validated substance/substance group **Peppermint oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30930-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Peppermint oil            | 4      | 5      | 67     |

## 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 54 961 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.
- 24 545 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 761 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.

- 107 spectra from 74 *Apo-Ident* customers from 68 batches from the substance/substance group *Peppermint oil*.
- Among them are spectra of independent samples from 67 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier  | Substance      | Batch        | Spectra |
|-----------|----------------|--------------|---------|
| 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       |
| 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       |
| Euro OTC  | Peppermint oil | 180400802    | 1       |

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| Supplier          | Substance      | Batch                | Spectra |
|-------------------|----------------|----------------------|---------|
| 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       |
| Caelo             | Peppermint oil | 18000796             | 1       |
| Kögl              | Peppermint oil | 421211154615         | 1       |
| Melsan            | Peppermint oil | 1705811              | 1       |
| Euro OTC          | Peppermint oil | 1804008-02           | 1       |
| Ph/Euro           | Peppermint oil | 170303202            | 1       |
| Phoenix           | Peppermint oil | 19135905             | 1       |
| Phoenix 28.12..18 | Peppermint oil | 18221702             | 1       |
| Caelo             | Peppermint oil | 19135905             | 3       |
| Bombastus         | Peppermint oil | 18005114             | 3       |
| 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 | 63561-126008         | 2       |
| Taoasis           | Peppermint oil | 63561-125729         | 1       |
| Taoasis           | Peppermint oil | 65074-125102BAG90451 | 1       |
| Taoasis           | Peppermint oil | 52216-123564         | 1       |
| Taoasis           | Peppermint oil | 63561-125104         | 1       |
| Taoasis           | Peppermint oil | 75404-127882         | 1       |
| Taoasis           | Peppermint oil | 79725-126853         | 1       |
| Taoasis           | Peppermint oil | 79725-12653          | 1       |
| Taoasis           | Peppermint oil | 79725-128653         | 2       |
| Taoasis           | Peppermint oil | 78725-128653         | 1       |
| 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       |

- 9188 spectra from 767 *Apo-Ident* customers from a total of 3608 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              | 24 545        |
| Type B | 0              | 190           | 10             | 20 761        |
| Type C | 0              | 103           | 4              | 9188          |

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 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| Type B | 100.0000 % (> 99.9454 %) | 95.0000 % (> 93.5000 %)  |
| Type C | 100.0000 % (> 98.7985 %) | 96.2617 % (> 93.4579 %)  |

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

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

Where the number of spectra does 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 | 67.52                  | –                              |

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                         | 87.93                           |
| 30965     | 30965               | 0.00                         | 92.65                           |
| 32481     | 32481               | 0.00                         | 72.74                           |
| 33809     | 33809               | 0.00                         | 69.35                           |

The identity of a sample will be confirmed by NIR if the distance to the next foreign sample is at least 50 % greater than the distance to a reference sample whose identity has been established by

laboratory testing. This criterion is always considered in the chemometric model, which contains all substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Perfume oil vanilla**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30665-2021-06-11  
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/substance group | 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 54 961 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.
- 24 525 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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       |

- 9280 spectra from 772 *Apo-Ident* customers from a total of 3673 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 180           | 0              | 24 525        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 15            | 0              | 9280          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.6667 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8022 %) | 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<br>main model | Distance in<br>second-stage model |
|------------|---------------------------|-----------------------------------|
| Salmon oil | 97.78                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30665     | 30665                  | 0.00                            | 123.63                             |
| 31191     | 31191                  | 0.00                            | 120.85                             |
| 31400     | 31400                  | 0.00                            | 121.55                             |
| 31786     | 31786                  | 0.00                            | 129.74                             |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Raspberry aroma**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30562-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Raspberry aroma           | 3      | 4      | 63     |

## 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 54 961 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.
- 24 585 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 447 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.

- 240 spectra from 132 *Apo-Ident* customers from 66 batches from the substance/substance group *Raspberry aroma*.
- 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 |
|-----------|-----------------|-------------|---------|
| Caelo     | Raspberry aroma | 12054311    | 1       |
| Anzag06.  | Raspberry aroma | 14376109    | 1       |
| Bombastus | Raspberry aroma | 12246608    | 1       |
| Caelo     | Raspberry aroma | 11303813    | 1       |
| Caelo     | Raspberry aroma | 12054310    | 1       |
| Caelo     | Raspberry aroma | 12246608    | 2       |
| Caelo     | Raspberry aroma | 12054302    | 1       |
| Caelo     | Raspberry aroma | 12246604    | 1       |
| Caelo     | Raspberry aroma | 13255502    | 2       |
| Caelo     | Raspberry aroma | 13255510    | 1       |
| Caelo     | Raspberry aroma | 14376109    | 4       |
| Caelo     | Raspberry aroma | 14376103    | 2       |
| Caelo     | Raspberry aroma | 15438503    | 8       |
| Caelo     | Raspberry aroma | 16126602    | 3       |
| Caelo     | Raspberry aroma | 16126606    | 2       |
| Caelo     | Raspberry aroma | 17187202    | 4       |
| Caelo     | Raspberry aroma | 17187205    | 8       |
| 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 | 19160001    | 3       |
| Caelo     | Raspberry aroma | 18249911    | 1       |
| Caelo     | Raspberry aroma | 20002006003 | 2       |
| Caelo     | Raspberry aroma | 192776      | 2       |
| Caelo     | Raspberry aroma | 20002006002 | 1       |
| Caelo     | Raspberry aroma | 19160006    | 2       |
| Caelo     | Raspberry aroma | 18074307    | 13      |
| Caelo     | Raspberry aroma | 17187201    | 1       |
| Caelo     | Raspberry aroma | 14376115    | 5       |
| 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       |

*continued on the next page*



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| Supplier                   | Substance       | Batch       | Spectra |
|----------------------------|-----------------|-------------|---------|
| Caelo                      | Raspberry aroma | 17258107    | 3       |
| Caelo                      | Raspberry aroma | 19160002    | 11      |
| Caelo                      | Raspberry aroma | 17187213    | 1       |
| Caelo                      | Raspberry aroma | 14115909    | 1       |
| Caelo                      | Raspberry aroma | 15219102    | 3       |
| 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 | 20002006003 | 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       |
| Caelo                      | Raspberry aroma | 192776010   | 2       |
| Noweda                     | Raspberry aroma | 14115909    | 1       |
| Noweda                     | Raspberry aroma | 18249905    | 1       |
| Noweda/ Caesar&Lorenz G... | Raspberry aroma | 192776001   | 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       |

- 9055 spectra from 755 *Apo-Ident* customers from a total of 3609 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 24 585        |
| <b>Type B</b> | 0              | 157           | 3              | 20 801        |
| <b>Type C</b> | 0              | 233           | 7              | 9055          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 98.1250 % (> 96.2500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7982 %) | 97.0833 % (> 95.8333 %)  |

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

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

Where the number of spectra does 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 | 58.23                  | —                              |

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                         | 63.81                           |
| 31396     | 31396               | 0.00                         | 68.02                           |
| 33222     | 33222               | 0.00                         | 75.22                           |

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 2.4-2021-02

Validated substance/substance group **Ravensara oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30386-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Ravensara oil; Ravensara (essentiell 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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 448 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 | 231012-119831  | 1       |
| Taoasis  | Ravensara oil | 9331006-121650 | 3       |
| Taoasis  | Ravensara oil | 231012-120291  | 1       |
| Taoasis  | Ravensara oil | 1687-125316    | 1       |
| Taoasis  | Ravensara oil | 1687-126824    | 1       |
| Taoasis  | Ravensara oil | 1687-127661    | 1       |
| Taoasis  | Ravensara oil | 59/144/17      | 1       |
| Taoasis  | Ravensara oil | 1944-1733      | 1       |
| Taoasis  | Ravensara oil | 1994-3103      | 1       |
| Taoasis  | Ravensara oil | 2427-5280      | 1       |
| Taoasis  | Ravensara oil | 1944-1388      | 1       |
| Taoasis  | Ravensara oil | 231012-118739  | 2       |

- 9275 spectra from 772 *Apo-Ident* customers from a total of 3660 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 160           | 0              | 20 801        |
| <b>Type C</b> | 0              | 20            | 0              | 9275          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 96.2500 %) |
| <b>Type C</b> | 100.0000 % (> 98.8011 %) | 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                | 23.04                  | —                              |
| Sage oil                  | 25.72                  | —                              |
| Citrus oil                | 28.14                  | —                              |
| Rosemary camphor oil      | 34.24                  | —                              |
| Angelica root oil         | 35.88                  | —                              |
| Myrtle oil                | 40.37                  | —                              |
| Yarrow oil                | 41.77                  | —                              |
| Marjoram oil              | 42.15                  | —                              |
| Rosemary oil              | 42.53                  | —                              |
| Eucalyptus oil            | 44.85                  | —                              |
| Niaouli oil               | 45.56                  | —                              |
| Cajeput (essentielle oil) | 46.87                  | —                              |

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                         | 23.04                           |
| 33854     | 33854               | 0.00                         | 25.67                           |
| 33872     | 33872               | 0.00                         | 24.32                           |

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

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





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Rose-geranium oil, organic**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30536-2021-06-11  
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/substance group  | 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 54 961 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.
- 24 485 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20841 spectra from a total of 448 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 | 130111-110467   | 1       |
| Taoasis             | Rose-geranium oil, organic | 130729-113060   | 1       |
| Taoasis             | Rose-geranium oil, organic | 130111-112615   | 1       |
| Taoasis             | Rose-geranium oil, organic | 401011-117806   | 2       |
| Taoasis             | Rose-geranium oil, organic | 401011-117641   | 1       |
| Taoasis             | Rose-geranium oil, organic | 21027-119121    | 1       |
| Taoasis             | Rose-geranium oil, organic | 21027-121337    | 1       |
| Taoasis             | Rose-geranium oil, organic | 21027-120292    | 1       |
| Taoasis             | Rose-geranium oil, organic | 1500969-123554  | 1       |
| Taoasis             | Rose-geranium oil, organic | A1616008-128497 | 1       |
| Taoasis             | Rose-geranium oil, organic | 1840-374        | 2       |
| Taoasis             | Rose-geranium oil, organic | 1840-128860     | 2       |
| Taoasis             | Rose-geranium oil, organic | 2445-3947       | 3       |
| Taoasis             | Rose-geranium oil, organic | 2445-6615       | 1       |
| Taoasis             | Rose-geranium oil, organic | 2445-3346       | 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       |

- 9265 spectra from 772 *Apo-Ident* customers from a total of 3650 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              | 24 485        |
| Type B | 0              | 120           | 0              | 20 841        |
| Type C | 0              | 30            | 0              | 9265          |

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 % (> 99.9603 %) | 100.0000 % (> 97.2727 %) |
| Type B | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| Type C | 100.0000 % (> 98.8001 %) | 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                         | 24.43                  | —                              |
| alpha-bisabolol (racemic) at least 85% | 33.30                  | —                              |
| Marjoram oil                           | 49.93                  | —                              |
| Carrot seed oil                        | 53.04                  | —                              |

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                         | 33.11                           |
| 31776     | 31776               | 0.00                         | 34.12                           |
| 31951     | 31951               | 0.00                         | 33.79                           |
| 33036     | 33036               | 0.00                         | 27.64                           |

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 2.4-2021-02

Validated substance/substance group **Rosemary camphor oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33803-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------------|---------------------------|-----------------------------------|
| Rosemary oil            | 19.85                     | —                                 |
| Eucalyptus oil          | 21.24                     | —                                 |
| Citrus oil              | 26.97                     | —                                 |
| Hyssop oil              | 27.01                     | —                                 |
| Niaouli oil             | 29.37                     | —                                 |
| Ravensara oil           | 32.21                     | —                                 |
| Cajeput (essentiel oil) | 34.87                     | —                                 |
| Sage oil                | 37.23                     | —                                 |
| Myrtle oil              | 47.10                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33803     | 33803                  | 0.00                            | 20.27                              |
| 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 2.4-2021-02

Validated substance/substance group **Rosewood oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31556-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 449 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 | 5101015-124243  | 1       |
| Taoasis               | Rosewood oil | 5101015-124967  | 3       |
| Taoasis               | Rosewood oil | 42543-126343    | 1       |
| Taoasis               | Rosewood oil | 42543-128666    | 1       |
| Taoasis               | Rosewood oil | 42543-128055    | 2       |
| Taoasis               | Rosewood oil | 42543-127664    | 1       |
| Taoasis               | Rosewood oil | 42543-146       | 4       |
| Taoasis               | Rosewood oil | 42543-2053      | 2       |
| Taoasis               | Rosewood oil | 9177-3983       | 2       |
| Taoasis               | Rosewood oil | 109177-5788     | 4       |
| Taoasis GmbH/ Taoasis | Rosewood oil | 109177-5788     | 1       |
| Taoasis/Taoasis       | Rosewood oil | 109177-5863     | 1       |

- 9264 spectra from 772 *Apo-Ident* customers from a total of 3659 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 120           | 0              | 20 819        |
| <b>Type C</b> | 0              | 31            | 0              | 9264          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9458 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8000 %) | 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.

| <b>Substance</b> | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|------------------|-------------------------------|---------------------------------------|
| Thyme oil, white | 39.58                         | –                                     |
| Coriander oil    | 58.89                         | –                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31556            | 31556                      | 0.00                                | 44.06                                  |
| 31688            | 31688                      | 0.00                                | 50.38                                  |
| 34106            | 34106                      | 0.00                                | 39.58                                  |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Sage oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31139-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Sage oil                  | 3      | 1      | 13     |



## 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |



- 20 881 spectra from a total of 450 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.

- 17 spectra from 5 *Apo-Ident* customers from 13 batches from the substance/substance group *Sage oil*.
- 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 |
|----------------------------|-----------|----------------|---------|
| Bombastus                  | Sage oil  | 309857         | 1       |
| Bombastus                  | Sage oil  | 18004276       | 2       |
| Taoasis                    | Sage oil  | 13988-117449   | 1       |
| Taoasis                    | Sage oil  | 29944-120889   | 1       |
| Taoasis                    | Sage oil  | 21190-118009   | 1       |
| Taoasis                    | Sage oil  | 21190-119239   | 1       |
| Taoasis                    | Sage oil  | 29944-120965   | 1       |
| Taoasis                    | Sage oil  | 8461016-127221 | 1       |
| Taoasis                    | Sage oil  | 8461016-774    | 2       |
| Taoasis                    | Sage oil  | 8461016-3526   | 2       |
| Taoasis                    | Sage oil  | 8461016-2158   | 1       |
| Taoasis                    | Sage oil  | 461016-6429    | 2       |
| Taoasis/Phoenix/22.03.2... | Sage oil  | 7156ITL06      | 1       |

- 9278 spectra from 772 *Apo-Ident* customers from a total of 3663 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 140           | 0              | 24 565        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 15            | 2              | 9278          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8017 %) | 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.

| <b>Substance</b>      | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|-----------------------|-------------------------------|---------------------------------------|
| Rosemary camphor oil  | 23.01                         | —                                     |
| Eucalyptus oil        | 31.50                         | —                                     |
| Matricaria oil, roman | 35.59                         | —                                     |
| Hyssop oil            | 36.64                         | —                                     |
| Rosemary oil          | 38.76                         | —                                     |
| Ravensara oil         | 39.04                         | —                                     |
| Silver fir oil        | 45.26                         | —                                     |
| Citrus oil            | 53.21                         | —                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31139            | 31139                      | 0.00                                | 36.64                                  |
| 31257            | 31257                      | 0.00                                | 36.70                                  |
| 31783            | 31783                      | 0.00                                | 31.61                                  |

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

variance of the original reference substance, but cannot add new aspects or forms of the substance.



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Salicylic white paraffin 10%**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31521-2021-06-11  
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/substance group    | 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 54 961 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.
- 24 530 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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.

- 14 spectra from 11 *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% | 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% | 19140601 | 2       |
| Caelo                 | Salicylic white paraffin 10% | 18245603 | 1       |
| Eigenrezeptur         | Salicylic white paraffin 10% | 150702   | 1       |
| Winthrop Arzneimittel | Salicylic white paraffin 10% | IE6931   | 1       |

- 9281 spectra from 771 *Apo-Ident* customers from a total of 3663 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 175           | 0              | 24 530        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 14            | 0              | 9281          |

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 % (> 99.9604 %) | 100.0000 % (> 96.5714 %) |
| Type B | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| Type C | 100.0000 % (> 98.8025 %) | 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)         | 46.19                  | —                              |
| Neribas <sup>®</sup> fat ointment | 48.93                  | —                              |
| Cottonwood ointment               | 52.90                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31521     | 31521               | 0.00                         | 62.81                           |
| 31629     | 31629               | 0.00                         | 62.52                           |
| 33473     | 33473               | 0.00                         | 62.19                           |

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 2.4-2021-02

Validated substance/substance group **Salmon oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33088-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-----------------|---------------------------|-----------------------------------|
| Argan oil       | 47.89                     | —                                 |
| Balm Bio Nature | 54.02                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33088     | 33088                  | 0.00                            | 45.32                              |
| 34225     | 34225                  | 0.00                            | 51.31                              |

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 2.4-2021-02

Validated substance/substance group **Sandalwood oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33799-2021-06-11  
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/substance group | 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 54 961 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.
- 24 585 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 120           | 0              | 24 585        |
| <b>Type B</b> | 0              | 120           | 0              | 20 841        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9606 %) | 100.0000 % (> 95.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------|---------------------------|-----------------------------------|
| Savory herb | 113.78                    | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33799     | 33799                  | 0.00                            | 129.01                             |
| 33801     | 33801                  | 0.00                            | 138.62                             |
| 33832     | 33832                  | 0.00                            | 130.03                             |

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 2.4-2021-02

Validated substance/substance group **Savory herb**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33820-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Thyme oil, red | 23.59                     | —                                 |
| Oregano oil    | 41.07                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33820     | 33820                  | 0.00                            | 25.90                              |
| 33821     | 33821                  | 0.00                            | 23.59                              |

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 2.4-2021-02

|                                     |                                                                                      |
|-------------------------------------|--------------------------------------------------------------------------------------|
| Validated substance/substance group | Sebexol <sup>®</sup> formula basis / Sebexol <sup>®</sup> cream lotion / Wofacutan w |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                                         |
| Report date                         | 11/06/2021                                                                           |
| Report number                       | 30839-2021-06-11                                                                     |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>Germany                      |

### Relevant substance names

Sebexol<sup>®</sup> formula basis / Sebexol<sup>®</sup> cream lotion / Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver; Hans Karrer Hydrocream MicroSilver; Sebexol<sup>®</sup> basic pH 5 formula basis; Sebexol<sup>®</sup> cream lotion pH 5; Wofacutan wash lotion

### Special notes

When selecting the *Sebexol<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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 | <i>European Pharmacopoeia 10th Edition, Basic Version 2020</i> [3] |
| Komm2.2.40        | <i>Erfüllung von Ph. Eur. 2.2.40 durch Apo-Ident</i> [4]           |
| AA004             | <i>Erstellung und Validierung eines IdentModul-Updates</i>         |

### Validation method

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

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

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

### Number of independent samples (batches) in calibration and validation

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

| Substance/substance group                                                                                                                 | Type A | Type B | Type C |
|-------------------------------------------------------------------------------------------------------------------------------------------|--------|--------|--------|
| Sebexol <sup>®</sup> formula basis / Sebexol <sup>®</sup> cream lotion<br>/ Wofacutan washing lotion / Hans Karrer Hydrocream MicroSilver | 14     | 6      | 172    |

## Second-stage model

For differentiation of the substance/substance group *Sebexol<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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 <sup>®</sup> basic p... | 1307    | 31104     | 40      | 1403098      |
| Devesa           | Sebexol <sup>®</sup> basic p... | 1522    | 31961     | 60      | not required |
| Devesa           | Sebexol <sup>®</sup> basic p... | 1638124 | 32744     | 40      | not required |
| Devesa           | Sebexol <sup>®</sup> cream l... | 1220    | 30839     | 40      | 1403097      |
| Devesa           | Sebexol <sup>®</sup> cream l... | 1317    | 31103     | 40      | not required |
| Devesa           | Sebexol <sup>®</sup> cream l... | 1412    | 31592     | 45      | not required |
| Devesa           | Sebexol <sup>®</sup> cream l... | 1531    | 31839     | 60      | not required |
| Devesa           | Sebexol <sup>®</sup> 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 54 961 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<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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.
- 24 060 spectra from a total of 496 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      |

- 20641 spectra from a total of 445 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.

- 869 spectra from 133 *Apo-Ident* customers from 171 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 144 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... | L0T19001 | 1       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 18003    | 4       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 18001    | 1       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 19001    | 5       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 18004    | 1       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 19003    | 3       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 20001    | 1       |
| Hans Karrer/Phönix    | Hans Karrer Hydrocream Micro... | 20005    | 1       |
| 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       |

*continued on the next page*



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| Supplier        | Substance                                   | Batch           | Spectra |
|-----------------|---------------------------------------------|-----------------|---------|
| Bombastus       | Sebexol <sup>®</sup> basic pH 5 formula ... | 1346            | 2       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1746116         | 2       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440            | 1       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127         | 2       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1239            | 1       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117         | 2       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119         | 2       |
| Caelo           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107         | 1       |
| Deversa/Noweda  | Sebexol <sup>®</sup> basic pH 5 formula ... | 2031128         | 1       |
| devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111         | 3       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | I307            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | I232            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1239            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1232            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328            | 5       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1335            | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1404            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1407            | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440            | 4       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1511            | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1543            | 5       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127         | 4       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1430            | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1683124         | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117         | 1       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102         | 3       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122         | 3       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111         | 3       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113         | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110         | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119         | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1912118         | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107         | 2       |
| Devesa          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1946114         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1318            | 2       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328            | 2       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440            | 2       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1511            | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113         | 3       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1912118         | 1       |
| DEVESA          | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126         | 1       |
| Devesa / Gehe   | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126         | 1       |
| Devesa / Kehr   | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102         | 1       |
| Devesa / Noweda | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117         | 1       |
| Devesa / Noweda | Sebexol <sup>®</sup> basic pH 5 formula ... | 1638124         | 1       |
| Devesa / Noweda | Sebexol <sup>®</sup> basic pH 5 formula ... | 170420S/1620117 | 1       |
| Devesa / Noweda | Sebexol <sup>®</sup> basic pH 5 formula ... | 170516S/1644102 | 1       |
| DEVESA / Noweda | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122         | 3       |

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| Supplier                   | Substance                                   | Batch      | Spectra |
|----------------------------|---------------------------------------------|------------|---------|
| DEVESA /G                  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1912118    | 1       |
| Devesa Dr. Reingraber G... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110    | 1       |
| Devesa Dr. Reingraber G... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107    | 2       |
| Devesa Dr.Reingraber GmbH  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1425       | 1       |
| DEVESA Dr.Reingraber GmbH  | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328       | 1       |
| Devesa Dr.Reingraber Gm... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1244       | 1       |
| Devesa Dr.Reingraber Gm... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1303       | 1       |
| Devesa Dr.Reingraber Gm... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126    | 1       |
| Devesa Dr.Reingraber Gm... | Sebexol <sup>®</sup> basic pH 5 formula ... | 2031128    | 1       |
| Devesa- Phönix             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127    | 1       |
| Devesa/ Noweda             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122    | 1       |
| Devesa/ Ebert              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126    | 1       |
| Devesa/ Fiebig             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1338       | 1       |
| Devesa/ Phoenix            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1543       | 1       |
| Devesa/AHD                 | Sebexol <sup>®</sup> basic pH 5 formula ... | 1245       | 4       |
| Devesa/AHD                 | Sebexol <sup>®</sup> basic pH 5 formula ... | 1131       | 2       |
| Devesa/AHD                 | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328       | 7       |
| Devesa/Alliance            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1946114    | 2       |
| Devesa/Alliance            | Sebexol <sup>®</sup> basic pH 5 formula ... | 2009126    | 2       |
| devesa/gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1346       | 1       |
| devesa/gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1356       | 1       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119    | 1       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1912118    | 1       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107    | 2       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126    | 2       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1946114    | 1       |
| Devesa/Kehr                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1407       | 2       |
| Devesa/Kehr                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117    | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1430       | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440       | 2       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1638124    | 2       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127    | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111/05 | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113    | 2       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110    | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1946114    | 2       |
| DEVESA/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127    | 1       |
| DEVESA/Noweda              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1543       | 1       |
| Devesa/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1543       | 3       |
| Devesa/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117    | 2       |
| Devesa/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122    | 2       |
| Devesa/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 2031128    | 2       |
| DEVESA/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111    | 1       |
| DEVESA/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113    | 1       |
| DEVESA/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110    | 1       |
| DEVESA/Phönix              | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440       | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1522       | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1543       | 4       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1638124    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102    | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1712122    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1807113    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126    | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1746116    | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 187126/06  | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110    | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1851119    | 1       |

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| Supplier                   | Substance                                   | Batch       | Spectra |
|----------------------------|---------------------------------------------|-------------|---------|
| Devesa/Sanacorp            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126     | 1       |
| Dr Reinhard GmbH- Kehr     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1620117     | 1       |
| Dr. Reingraber GmbH        | Sebexol <sup>®</sup> basic pH 5 formula ... | 1708120     | 1       |
| Dr.Reingraber GmbH         | Sebexol <sup>®</sup> basic pH 5 formula ... | 1232        | 1       |
| Dr.Reingraber/sanacorp     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111     | 1       |
| Dr.Reingraber/sanacorp     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1923107     | 1       |
| Eigenherstellung           | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328        | 1       |
| Fagron                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1425        | 1       |
| Fagron                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1510        | 2       |
| Fiebig                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1511        | 2       |
| Gehe                       | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126     | 2       |
| Holdermann                 | Sebexol <sup>®</sup> basic pH 5 formula ... | 1307        | 1       |
| Ichthyol                   | Sebexol <sup>®</sup> basic pH 5 formula ... | 1232        | 2       |
| Kehr/ Devesa               | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102     | 1       |
| Kehr/ Devesa               | Sebexol <sup>®</sup> basic pH 5 formula ... | 1746116     | 4       |
| Kehr/Devesa                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1817126     | 2       |
| Kehr/Devesa                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1828110     | 2       |
| noweda                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 2009126     | 1       |
| Noweda                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1328        | 1       |
| Noweda / Dewesa            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1719111     | 1       |
| Noweda /Devesa             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102     | 3       |
| Noweda/Devesa              | Sebexol <sup>®</sup> basic pH 5 formula ... | 2x1407      | 1       |
| Phoenix                    | Sebexol <sup>®</sup> basic pH 5 formula ... | 1440        | 1       |
| Phoenix/Devesa             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1215        | 1       |
| Phoenix/Devesa             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1407        | 1       |
| Phoenix/Devesa             | Sebexol <sup>®</sup> basic pH 5 formula ... | 1604127     | 1       |
| Phönix                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1313        | 2       |
| Phönix                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1416        | 1       |
| Phönix                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1425        | 2       |
| Phönix / Devesa            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1644102     | 1       |
| Phönix, Devesa, 29.09.2... | Sebexol <sup>®</sup> basic pH 5 formula ... | 2009126     | 1       |
| Phönix/ Devesa, 14.12.2... | Sebexol <sup>®</sup> basic pH 5 formula ... | 1935126     | 3       |
| Sanacorp                   | Sebexol <sup>®</sup> basic pH 5 formula ... | 1313        | 1       |
| Sebexol                    | Sebexol <sup>®</sup> basic pH 5 formula ... | 1333        | 1       |
| Sebexol                    | Sebexol <sup>®</sup> basic pH 5 formula ... | 1313        | 1       |
| Sebexol/ Noweda            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1403        | 1       |
| Sebexol/ Noweda            | Sebexol <sup>®</sup> basic pH 5 formula ... | 1430        | 1       |
| Sebexol/AHD                | Sebexol <sup>®</sup> basic pH 5 formula ... | 1303        | 2       |
| Astellas                   | Sebexol <sup>®</sup> cream lotion pH 5      | 1504        | 2       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1511        | 2       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1417        | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1504        | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 4117E-03872 | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1604129     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1605101     | 3       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1727207     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1807113     | 2       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1812123     | 2       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1828110     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1836106     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 19031605    | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1531        | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1912119     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1736105     | 3       |
| deversa                    | Sebexol <sup>®</sup> cream lotion pH 5      | 1935227     | 5       |
| Deversa/Fiebig             | Sebexol <sup>®</sup> cream lotion pH 5      | 1817127     | 1       |
| Deversa/Fiebig             | Sebexol <sup>®</sup> cream lotion pH 5      | 1824115     | 1       |
| devesa                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1746116     | 1       |
| Devesa                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1510        | 4       |
| Devesa                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1523        | 3       |

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| Supplier        | Substance                              | Batch           | Spectra |
|-----------------|----------------------------------------|-----------------|---------|
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1524            | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1604128         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120         | 3       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1417N-03872     | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1651121         | 2       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1727107         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1746116         | 4       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1743225         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108/01      | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1817127         | 2       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1604328         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223         | 5       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1824115         | 3       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102         | 3       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120         | 2       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127         | 2       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108/06-2022 | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120         | 2       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 2019107         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 2019207         | 1       |
| Devesa          | Sebexol <sup>®</sup> cream lotion pH 5 | 2040130         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1505            | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1510            | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1523            | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1531            | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1651120         | 2       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1736105         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108/01      | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1743225         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1812123         | 2       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1836106         | 2       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103         | 1       |
| DEVESA          | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227         | 2       |
| Devesa /        | Sebexol <sup>®</sup> cream lotion pH 5 | 1511            | 1       |
| Devesa /        | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223         | 1       |
| Devesa /        | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119         | 1       |
| Devesa /        | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108         | 2       |
| Devesa / AHD    | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118         | 1       |
| Devesa / AHD    | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227         | 1       |
| Devesa / AHD    | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227         | 2       |
| DEVESA / Anzag  | Sebexol <sup>®</sup> cream lotion pH 5 | 1605101         | 1       |
| DEVESA / Anzag  | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208         | 1       |
| devesa / Fiebig | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106         | 1       |
| devesa / Fiebig | Sebexol <sup>®</sup> cream lotion pH 5 | 1743125         | 1       |
| devesa / Fiebig | Sebexol <sup>®</sup> cream lotion pH 5 | 1746116         | 1       |

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| Supplier                   | Substance                              | Batch                | Spectra |
|----------------------------|----------------------------------------|----------------------|---------|
| devesa / Fiebig            | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208              | 1       |
| devesa / Fiebig            | Sebexol <sup>®</sup> cream lotion pH 5 | 1812123              | 1       |
| devesa / Fiebig            | Sebexol <sup>®</sup> cream lotion pH 5 | 1828110              | 1       |
| devesa / Fiebig            | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120              | 1       |
| devesa / Fiebig            | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227              | 1       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1517                 | 1       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1530                 | 2       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1651120              | 1       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1727107              | 1       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106              | 2       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1746116              | 3       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215              | 2       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108              | 1       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127              | 1       |
| Devesa / Gehe 08.12.18     | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215-S20190115Ma7 | 1       |
| Devesa / Gehe 15.3.18      | Sebexol <sup>®</sup> cream lotion pH 5 | 1743225-20180404Ma10 | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1430                 | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1531                 | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1644102              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1712223              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106              | 2       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1720115              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1836105              | 3       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 2019207              | 3       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 2045106              | 1       |
| Devesa / Phönix            | Sebexol <sup>®</sup> cream lotion pH 5 | 1812123              | 1       |
| Devesa / Phönix            | Sebexol <sup>®</sup> cream lotion pH 5 | 2009127              | 1       |
| Devesa / Phönix            | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120              | 1       |
| Devesa / Sanacorp          | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111              | 2       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103              | 1       |
| Devesa / Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103              | 2       |
| Devesa / Phönix            | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113              | 9       |
| Devesa DR. Reingraber      | Sebexol <sup>®</sup> cream lotion pH 5 | 1651121              | 1       |
| Devesa Dr.Reingraben/Sa... | Sebexol <sup>®</sup> cream lotion pH 5 | 1743125              | 1       |
| Devesa Dr.Reingraben/Sa... | Sebexol <sup>®</sup> cream lotion pH 5 | 1817127              | 3       |
| Devesa Dr.Reingraber GmbH  | Sebexol <sup>®</sup> cream lotion pH 5 | 174611650ml          | 1       |
| Devesa Dr.Reingraber GmbH  | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127              | 1       |
| Devesa Dr.Reingraber GmbH  | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227              | 1       |
| Devesa Dr.Reingraber/Sa... | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121              | 1       |
| Devesa Dr.Reingraber/Sa... | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127              | 3       |
| Devesa GmbH /Alliance H... | Sebexol <sup>®</sup> cream lotion pH 5 | 1712223              | 1       |
| Devesa GmbH /Alliance H... | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111              | 1       |
| Devesa GmbH /Alliance H... | Sebexol <sup>®</sup> cream lotion pH 5 | 1828110              | 1       |
| devesa Noweda              | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208              | 1       |
| devesa phoenix             | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121              | 1       |
| devesa phoenix             | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119              | 1       |
| devesa phoenix             | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227              | 2       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1504                 | 2       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1524                 | 1       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1604129              | 4       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1644102              | 1       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 17433225             | 1       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118              | 1       |
| Devesa/ Noweda             | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227              | 1       |
| Devesa/ Fiebig             | Sebexol <sup>®</sup> cream lotion pH 5 | 1447                 | 1       |
| Devesa/ Fiebig             | Sebexol <sup>®</sup> cream lotion pH 5 | 1712223              | 2       |
| Devesa/ Fiebig             | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227              | 1       |

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| Supplier               | Substance                              | Batch      | Spectra |
|------------------------|----------------------------------------|------------|---------|
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1736105    | 1       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208    | 1       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113    | 1       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227    | 2       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103    | 1       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227    | 4       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118    | 1       |
| Devesa/ Noweda         | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119    | 2       |
| Devesa/ Phoenix        | Sebexol <sup>®</sup> cream lotion pH 5 | 1620117    | 1       |
| Devesa/ Phoenix        | Sebexol <sup>®</sup> cream lotion pH 5 | 1817127    | 1       |
| DEVESA/ Phoenix        | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127/09 | 1       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1524       | 1       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1727207    | 1       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1736105    | 2       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106    | 6       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1743225    | 2       |
| Devesa/ Phönix         | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223    | 3       |
| Devesa/ Sanacorp       | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121    | 1       |
| Devesa/ Sanacorp       | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108    | 1       |
| Devesa/ Sanacorp       | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120    | 1       |
| Devesa/ Sanacorp       | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127    | 1       |
| Devesa/ Sanacorp       | Sebexol <sup>®</sup> cream lotion pH 5 | 20042120   | 1       |
| Devesa/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1426       | 1       |
| Devesa/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1511       | 1       |
| Devesa/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1712123    | 2       |
| Devesa/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1736105    | 5       |
| Devesa/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1824115    | 2       |
| DEVESA/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121    | 1       |
| DEVESA/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127    | 1       |
| DEVESA/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118    | 1       |
| DEVESA/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227    | 1       |
| DEVESA/Fiebig          | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1504       | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1712123    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1644102    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1651121    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1836106    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119    | 1       |
| Devesa/Gehe            | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127    | 1       |
| Devesa/Kehr/25.05.2020 | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120    | 2       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108    | 1       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102    | 1       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118    | 1       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120    | 2       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227    | 1       |
| Devesa/Krieger         | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103    | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1504/01    | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1504       | 2       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1523       | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1552       | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1604228    | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1604129    | 1       |
| Devesa/NOW             | Sebexol <sup>®</sup> cream lotion pH 5 | 1644102    | 1       |
| Devesa/Noweda          | Sebexol <sup>®</sup> cream lotion pH 5 | 1447       | 3       |
| Devesa/Noweda          | Sebexol <sup>®</sup> cream lotion pH 5 | 1604228    | 6       |
| Devesa/Noweda          | Sebexol <sup>®</sup> cream lotion pH 5 | 1543       | 1       |
| Devesa/Noweda          | Sebexol <sup>®</sup> cream lotion pH 5 | 1604328    | 5       |
| Devesa/Noweda          | Sebexol <sup>®</sup> cream lotion pH 5 | 1605201    | 3       |

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| Supplier        | Substance                              | Batch      | Spectra |
|-----------------|----------------------------------------|------------|---------|
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1605103    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1651121    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1651120    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1712123    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1719112    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1736105    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1736106    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1720115    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1743225    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227    | 3       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1824115    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111    | 2       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127    | 2       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127    | 2       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1939227    | 2       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119    | 5       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227    | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119/11 | 1       |
| Devesa/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 2040130    | 2       |
| DEVESA/Noweda   | Sebexol <sup>®</sup> cream lotion pH 5 | 1605201    | 2       |
| Devesa/Phoenix  | Sebexol <sup>®</sup> cream lotion pH 5 | 1511       | 1       |
| Devesa/Phoenix  | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113    | 3       |
| Devesa/Phoenix  | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121    | 1       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1727107    | 1       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1743125    | 5       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1746116    | 8       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1802208    | 5       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215    | 2       |
| devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 18201402   | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1727207    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1746116    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1824115    | 5       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113    | 2       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111    | 19      |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102    | 2       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103    | 6       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1836105    | 2       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120    | 3       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108    | 9       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121    | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1935227    | 6       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1939127    | 7       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 1807113/02 | 1       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120    | 2       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227    | 5       |
| Devesa/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 19107      | 1       |
| DEVESA/Phönix   | Sebexol <sup>®</sup> cream lotion pH 5 | 185119     | 1       |
| Devesa/Sanacorp | Sebexol <sup>®</sup> cream lotion pH 5 | 1511       | 1       |
| Devesa/Sanacorp | Sebexol <sup>®</sup> cream lotion pH 5 | 1530       | 2       |
| Devesa/Sanacorp | Sebexol <sup>®</sup> cream lotion pH 5 | 1743125    | 1       |

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| Supplier                   | Substance                              | Batch                | Spectra |
|----------------------------|----------------------------------------|----------------------|---------|
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108              | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111              | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121              | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120              | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102              | 2       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1935127              | 1       |
| Devesa/Sanacorp            | Sebexol <sup>®</sup> cream lotion pH 5 | 1817127              | 1       |
| Devesa/Sanacorp WE: 09...  | Sebexol <sup>®</sup> cream lotion pH 5 | 1651121              | 1       |
| Devesa-Fa.Gehe             | Sebexol <sup>®</sup> cream lotion pH 5 | 1727207/-20180112Ma9 | 1       |
| Devesa-Fa.Gehe             | Sebexol <sup>®</sup> cream lotion pH 5 | 1824215-S20181115Ma2 | 1       |
| Devesea                    | Sebexol <sup>®</sup> cream lotion pH 5 | 1604128              | 1       |
| Divesa                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223              | 1       |
| Dr. Reingraber GmbH        | Sebexol <sup>®</sup> cream lotion pH 5 | 1605103              | 1       |
| Dr. Reingraber GmbH / F... | Sebexol <sup>®</sup> cream lotion pH 5 | 1824115              | 1       |
| Euro OTC                   | Sebexol <sup>®</sup> cream lotion pH 5 | 1727207              | 1       |
| Fagron                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1517                 | 1       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1605101              | 2       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108              | 1       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1812223              | 1       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111              | 1       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119              | 1       |
| Fiebig                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120              | 1       |
| Fiebig/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227              | 1       |
| Fiebig/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1836105              | 2       |
| Fiebig/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120              | 1       |
| Fiebig/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 2009127              | 1       |
| FIEBIG; HERSTELLER DEVE... | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120              | 1       |
| Gehe                       | Sebexol <sup>®</sup> cream lotion pH 5 | 1605103              | 1       |
| Gehe                       | Sebexol <sup>®</sup> cream lotion pH 5 | 1727107              | 1       |
| Geibo/Devesa               | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118              | 1       |
| Hedinger/Noweda            | Sebexol <sup>®</sup> cream lotion pH 5 | 18424115             | 1       |
| Kehr 14.08.2020            | Sebexol <sup>®</sup> cream lotion pH 5 | 2009227              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1651120              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1712223              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1802108              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1817227              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1828111              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1836105              | 2       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1901103              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1901102              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1912119              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121              | 2       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1912120              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 1947119              | 3       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 2004120              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 2019107              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 2019207              | 1       |
| Noweda                     | Sebexol <sup>®</sup> cream lotion pH 5 | 2046109              | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5 | 1712223              | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5 | 1708120              | 3       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5 | 1719112              | 1       |
| Noweda/devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1836106              | 1       |
| Noweda/devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1923108              | 1       |
| Noweda/devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1925121              | 1       |
| Noweda/devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1947118              | 3       |
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1530                 | 1       |
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5 | 1605201              | 1       |

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| Supplier                   | Substance                                   | Batch       | Spectra |
|----------------------------|---------------------------------------------|-------------|---------|
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1720115     | 1       |
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1638124     | 1       |
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1812123     | 1       |
| Noweda/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1923108     | 1       |
| Phoenix/Devesa             | Sebexol <sup>®</sup> cream lotion pH 5      | 1736105     | 1       |
| Phoenix/Devesa             | Sebexol <sup>®</sup> cream lotion pH 5      | 1812123     | 1       |
| Phönix                     | Sebexol <sup>®</sup> cream lotion pH 5      | 160422      | 1       |
| Phönix                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1604129     | 1       |
| Phönix                     | Sebexol <sup>®</sup> cream lotion pH 5      | 4217A-03872 | 1       |
| Phönix                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1828111     | 2       |
| Phönix                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1912120     | 1       |
| Phönix/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1712123     | 1       |
| Phönix/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1651121     | 1       |
| Phönix/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 1817227     | 2       |
| Phönix/Devesa              | Sebexol <sup>®</sup> cream lotion pH 5      | 182811      | 1       |
| Phönix/DEVESA              | Sebexol <sup>®</sup> cream lotion pH 5      | 1935127     | 1       |
| Römerapo.                  | Sebexol <sup>®</sup> cream lotion pH 5      | 1828110     | 1       |
| Rondell Apotheke           | Sebexol <sup>®</sup> cream lotion pH 5      | 1523        | 1       |
| Sana/Devesa                | Sebexol <sup>®</sup> cream lotion pH 5      | 1935127     | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      | 1430        | 1       |
| Sanacorp / Devesa          | Sebexol <sup>®</sup> cream lotion pH 5      | 1836106     | 1       |
| sanacorp, 27.9.16,4,312EUR | Sebexol <sup>®</sup> cream lotion pH 5      | 1604328     | 1       |
| Sebexol                    | Sebexol <sup>®</sup> cream lotion pH 5      | 1812123     | 1       |
| Taosis                     | Sebexol <sup>®</sup> cream lotion pH 5      | 1828110     | 1       |
| THC Pharma                 | Sebexol <sup>®</sup> 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 <sup>®</sup> basic pH 5 formula ... | 1307        | 5       |
| Devesa                     | Sebexol <sup>®</sup> basic pH 5 formula ... |             | 7       |
| Devesa                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1522        | 3       |
| Devesa                     | Sebexol <sup>®</sup> basic pH 5 formula ... | 1638124     | 2       |
| Devesa/Gehe                | Sebexol <sup>®</sup> basic pH 5 formula ... |             | 1       |
| Caelo                      | Sebexol <sup>®</sup> cream lotion pH 5      |             | 2       |
| Devesa / Gehe              | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| Devesa/                    | Sebexol <sup>®</sup> cream lotion pH 5      |             | 2       |
| Devesa/fiebig              | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| Devesa/NOW                 | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| Devesa/Noweda              | Sebexol <sup>®</sup> cream lotion pH 5      |             | 3       |
| Dr. Wolff                  | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| Gehe/Devesa                | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| NOWEDA / HERSTELLER: DE... | Sebexol <sup>®</sup> cream lotion pH 5      |             | 1       |
| Kesla Pharma/Noweda        | Wofacutan wash lotion                       |             | 2       |
| Kesla/Noweda               | Wofacutan wash lotion                       |             | 5       |

- 8426 spectra from 767 *Apo-Ident* customers from a total of 3504 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<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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<sup>®</sup> formula basis / Sebexol<sup>®</sup>*



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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 645           | 0              | 24 060        |
| <b>Type B</b> | 0              | 320           | 0              | 20 641        |
| <b>Type C</b> | 0              | 862           | 7              | 8426          |

The substance/substance group *Sebexol<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.0698 %) |
| <b>Type B</b> | 100.0000 % (> 99.9453 %) | 100.0000 % (> 98.1250 %) |
| <b>Type C</b> | 100.0000 % (> 98.7980 %) | 99.1945 % (> 98.8493 %)  |

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

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

Where the number of spectra does 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<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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 <sup>®</sup> U Hydrolotio        | 15.11                  | —                              |
| Fenistil <sup>®</sup> Gel                 | 24.14                  | —                              |
| Dimeticone ointment 10% SR                | 26.25                  | —                              |
| Amciderm <sup>®</sup> Base cream          | 35.18                  | —                              |
| SyrSpend <sup>®</sup> SF pH4 cherry aroma | 36.00                  | —                              |
| Linola <sup>®</sup> Sept                  | 36.33                  | —                              |
| Abitima <sup>®</sup> clinic face cream    | 37.75                  | —                              |
| Aloe vera gel, 10x concentrated           | 42.38                  | —                              |
| Base cream Taoasis                        | 42.61                  | —                              |
| Retterspitz external                      | 42.80                  | —                              |
| SyrSpend <sup>®</sup> SF pH4 aroma free   | 43.54                  | —                              |
| Water                                     | 48.55                  | —                              |
| Neuroderm <sup>®</sup> moisturising cream | 50.77                  | —                              |

The list stops after the first substance with a *Mahalanobis distance* greater than 50. If the substance/substance group *Sebexol<sup>®</sup> formula basis / Sebexol<sup>®</sup> 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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30839     | 30839               | 0.00                         | 21.43                           |
| 30972     | 30972               | 0.00                         | 21.91                           |
| 31065     | 31065               | 0.00                         | 23.46                           |
| 31103     | 31103               | 0.00                         | 20.66                           |
| 31104     | 31104               | 0.00                         | 18.31                           |
| 31592     | 31592               | 0.00                         | 19.84                           |
| 31839     | 31839               | 0.00                         | 17.59                           |
| 31961     | 31961               | 0.00                         | 16.86                           |
| 32743     | 32743               | 0.00                         | 20.78                           |
| 32744     | 32744               | 0.00                         | 16.83                           |
| 33190     | 33190               | 0.00                         | 23.41                           |
| 33191     | 33191               | 0.00                         | 21.85                           |
| 33483     | 33483               | 0.00                         | 23.36                           |
| 34116     | 34116               | 0.00                         | 20.37                           |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Siam benzoin**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31490-2021-06-11  
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/substance group | 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------------|---------------------------|-----------------------------------|
| Cinnamon bark oil, Ceylon | 105.06                    | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31490     | 31490                  | 0.00                            | 105.06                             |
| 31844     | 31844                  | 0.00                            | 197.50                             |
| 34388     | 34388                  | 0.00                            | 229.21                             |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Solutio Cordes®**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30996-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Solutio Cordes®           | 2      | 3      | 16     |

## Second-stage model

For differentiation of the substance/substance group *Solutio Cordes*<sup>®</sup> the following second-stage model is used:

*no second-stage model*

## Calibration samples

Only spectra which have been recorded by *HiperScan 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*<sup>®</sup>:

| Supplier | Substance                          | Batch  | Sample ID | Spectra | Certificate  |
|----------|------------------------------------|--------|-----------|---------|--------------|
| Ichthyol | <i>Solutio Cordes</i> <sup>®</sup> | 12B006 | 30996     | 40      | not required |
| Ichthyol | <i>Solutio Cordes</i> <sup>®</sup> | 13B001 | 31076     | 40      | not required |

## Validation samples

A total of 54 961 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*<sup>®</sup>. These samples are listed above in the [calibration samples](#) section. The reference samples come from 2 different batches.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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*<sup>®</sup>.
- 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 | <i>Solutio Cordes</i> <sup>®</sup> | 15B005 | 32065     | 60      |
| Ichthyol | <i>Solutio Cordes</i> <sup>®</sup> | 17B007 | 34361     | 40      |
| Ichthyol | <i>Solutio Cordes</i> <sup>®</sup> | 19B007 | 34845     | 40      |
| Ichthyol | <i>Solutio Cordes</i> <sup>®</sup> | 15B005 | 32483     | 40      |



- 20 781 spectra from a total of 448 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 / E               | Solutio Cordes® | 15B005  | 3       |
| Ichthyol / G               | Solutio Cordes® | 14B012  | 1       |
| Ichthyol / G               | Solutio Cordes® | 16B005  | 3       |
| Ichthyol / Gehe            | Solutio Cordes® | 14B006  | 1       |
| Ichthyol /Noweda           | Solutio Cordes® | 12B005  | 1       |
| Ichthyol /Noweda           | Solutio Cordes® | 13B002  | 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® | 18B004  | 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       |

- 9229 spectra from 771 *Apo-Ident* customers from a total of 3655 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*<sup>®</sup> can clearly be 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*<sup>®</sup> and it was evaluated how many matches (positive) and rejections (negative) were correct or incorrect. The following table breaks down the numbers of correct and incorrect results according to 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              | 24 625        |
| Type B | 0              | 180           | 0              | 20 781        |
| Type C | 0              | 62            | 4              | 9229          |

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

|        | Specificity              | Recognition rate         |
|--------|--------------------------|--------------------------|
| Type A | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| Type B | 100.0000 % (> 99.9454 %) | 100.0000 % (> 96.6667 %) |
| Type C | 100.0000 % (> 98.7989 %) | 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*<sup>®</sup> 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 <sup>®</sup> moisturising cream | 71.03                  | —                              |

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

## Identity according to identity test using NIR spectroscopy

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

reference sample, in the following table the *Mahalanobis distance* to the reference sample is specified as well 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                         | 76.94                           |
| 31076     | 31076               | 0.00                         | 77.90                           |

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 2.4-2021-02

Validated substance/substance group **Spearmint oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30453-2021-06-11  
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/substance group | 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 54 961 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.
- 24 575 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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 | 27537-96244   | 1       |
| Taoasis  | Spearmint oil | 421012-125373 | 1       |
| Taoasis  | Spearmint oil | 106555-973    | 1       |
| Taoasis  | Spearmint oil | 106555-5139   | 1       |
| Taoasis  | Spearmint oil | 421012-123260 | 1       |

- 9290 spectra from 772 *Apo-Ident* customers from a total of 3670 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 130           | 0              | 24 575        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 5             | 0              | 9290          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9605 %) | 100.0000 % (> 95.3846 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8109 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------|---------------------------|-----------------------------------|
| Dwarf pine oil    | 48.38                     | –                                 |
| Angelica root oil | 55.31                     | –                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31135     | 31135                  | 0.00                            | 61.37                              |
| 31685     | 31685                  | 0.00                            | 57.93                              |
| 33481     | 33481                  | 0.00                            | 52.35                              |

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



# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31032-2021-06-11  
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/substance group                                                   | Type A | Type B | Type C |
|-----------------------------------------------------------------------------|--------|--------|--------|
| Spruce needle oil / Pine silvestris oil / Frankincense oil / Silver fir oil | 13     | 12     | 23     |

## 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 54 961 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.
- 24 075 spectra from a total of 496 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>†</sup> | 10      |
| Taoasis   | Silver fir oil      | 01A0B16-125623       | 33027              | 40      |

- 20 411 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.

- 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      | 30447-125444  | 1       |
| Taoasis               | Silver fir oil      | 212-120342    | 1       |
| Caelo                 | Spruce needle oil   | 10185604      | 1       |
| Caelo                 | Spruce needle oil   | 11324401      | 4       |
| Caelo                 | Spruce needle oil   | 13152001      | 2       |
| Primavera             | Spruce needle oil   | 1670814       | 1       |
| Taoasis               | Spruce needle oil   | 29828-107964  | 1       |
| Taoasis               | Spruce needle oil   | 531766-109893 | 1       |
| Taoasis               | Spruce needle oil   | 534474-111585 | 1       |

*continued on the next page*

<sup>†</sup>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 | 534374-22869  | 1       |
| Taoasis               | Spruce needle oil | 442-113922    | 1       |
| Taoasis               | Spruce needle oil | 1769-124969   | 2       |
| Taoasis               | Spruce needle oil | 1769-124949   | 1       |
| 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 | 534474-113171 | 1       |
| Taoasis/Sanacorp      | Spruce needle oil | 534474-111869 | 1       |
| Taoasis/Sanacorp      | Spruce needle oil | 11647-2942    | 1       |
| Apoth.Bauer&Co/Noweda | Frankincense oil  |               | 1       |

- 9263 spectra from 772 *Apo-Ident* customers from a total of 3651 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 630           | 0              | 24 075        |
| <b>Type B</b> | 0              | 403           | 147            | 20 411        |
| <b>Type C</b> | 0              | 17            | 15             | 9263          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9601 %) | 100.0000 % (> 99.0476 %) |
| <b>Type B</b> | 100.0000 % (> 99.9453 %) | 73.2727 % (> 72.7273 %)  |
| <b>Type C</b> | 100.0000 % (> 98.7999 %) | 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<br>main model | Distance in<br>second-stage model |
|-------------------|---------------------------|-----------------------------------|
| Swiss pine oil    | 12.33                     | —                                 |
| Spearmint oil     | 20.87                     | —                                 |
| Dwarf pine oil    | 26.76                     | —                                 |
| Angelica root oil | 26.97                     | —                                 |
| Ginger oil        | 29.50                     | —                                 |
| Citus oil         | 29.56                     | —                                 |
| Hyssop oil        | 32.42                     | —                                 |
| Citric oil        | 33.77                     | —                                 |
| Marjoram oil      | 34.60                     | —                                 |
| Juniper oil       | 38.19                     | —                                 |
| Cypress oil       | 40.44                     | —                                 |
| Myrtle oil        | 40.71                     | —                                 |
| Lime oil          | 41.62                     | —                                 |
| Cumin oil         | 49.12                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31032     | 31032                  | 0.00                            | 32.42                              |
| 31255     | 31255                  | 0.00                            | 35.07                              |
| 31633     | 31633                  | 0.00                            | 74.94                              |
| 31754     | 31754                  | 0.00                            | 21.97                              |
| 31819     | 31819                  | 0.00                            | 16.99                              |
| 32066     | 32066                  | 0.00                            | 19.57                              |
| 33052     | 33052                  | 0.00                            | 33.58                              |
| 33646     | 33646                  | 0.00                            | 13.63                              |
| 33650     | 33650                  | 0.00                            | 86.97                              |
| 33652     | 33652                  | 0.00                            | 84.95                              |
| 33726     | 33726                  | 0.00                            | 12.33                              |
| 33815     | 33815                  | 0.00                            | 15.81                              |
| 34177     | 34177                  | 0.00                            | 19.58                              |
| 34391     | 34391                  | 0.00                            | 41.62                              |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Stomahesive® adhesive paste</b>                              |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 30974-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group   | 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 54 961 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.
- 24 545 spectra from a total of 506 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      |



- 20 881 spectra from a total of 449 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 |
|------------------------|-----------------------------|-------|---------|
| Convatec               | Stomahesive® adhesive paste | 5G062 | 24      |
| Convatec Limited/ Gehe | Stomahesive® adhesive paste | 9B033 | 2       |
| ConvaTec/ Alliance     | Stomahesive® adhesive paste | 9K007 | 2       |
| Convatec/Gehe          | Stomahesive® adhesive paste | 9D046 | 1       |
| Convatec/Phönix        | Stomahesive® adhesive paste | 6D079 | 1       |

- 9265 spectra from 772 *Apo-Ident* customers from a total of 3670 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 30            | 0              | 9265          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8001 %) | 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% | 40.85                  | —                              |
| Lygal® ointment base      | 61.82                  | —                              |

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                         | 52.64                           |
| 31087     | 31087               | 0.00                         | 56.11                           |
| 33474     | 33474               | 0.00                         | 56.40                           |

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 2.4-2021-02

Validated substance/substance group **Strawberry aroma**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30643-2021-06-11  
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/substance group | Type A | Type B | Type C |
|---------------------------|--------|--------|--------|
| Strawberry aroma          | 3      | 4      | 26     |

## 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 54 961 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.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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*

continued from previous page

| 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      |

- 20 761 spectra from a total of 447 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.

- 84 spectra from 57 *Apo-Ident* customers from 28 batches from the substance/substance group *Strawberry aroma*.
- 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                      | 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  | 6       |
| Caelo                      | Strawberry aroma | 10803202  | 1       |
| Caelo                      | Strawberry aroma | 18083211  | 1       |
| Caelo                      | Strawberry aroma | 17024607  | 1       |
| Caelo                      | Strawberry aroma | 10184917  | 1       |
| Caelo                      | Strawberry aroma | 18083206  | 4       |
| 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 | 15411805  | 7       |
| Caelo                      | Strawberry aroma | 192763004 | 1       |
| 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       |

- 9211 spectra from 770 *Apo-Ident* customers from a total of 3647 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 200           | 0              | 20 761        |
| <b>Type C</b> | 0              | 83            | 1              | 9211          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 97.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.7987 %) | 98.8095 % (> 95.2381 %)  |

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

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

Where the number of spectra does 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 | 59.80                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 30643     | 30643               | 0.00                         | 97.89                           |
| 31395     | 31395               | 0.00                         | 79.61                           |
| 32814     | 32814               | 0.00                         | 91.37                           |
| 32838     | 32838               | 0.00                         | 65.71                           |

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





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Swiss pine oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31553-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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       |

- 9293 spectra from 772 *Apo-Ident* customers from a total of 3673 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 40            | 40             | 20 881        |
| <b>Type C</b> | 0              | 2             | 0              | 9293          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 50.0000 % (> 46.2500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8304 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Frankincense oil    | 14.26                     | —                                 |
| Pine silvestris oil | 19.24                     | —                                 |
| Spruce needle oil   | 20.58                     | —                                 |
| Angelica root oil   | 22.16                     | —                                 |
| Silver fir oil      | 23.44                     | —                                 |
| Dwarf pine oil      | 25.41                     | —                                 |
| Spearmint oil       | 26.35                     | —                                 |
| Ginger oil          | 31.87                     | —                                 |
| Citrus oil          | 34.15                     | —                                 |
| Cypress oil         | 38.14                     | —                                 |
| Marjoram oil        | 39.94                     | —                                 |
| Juniper oil         | 55.56                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31553     | 31553                  | 0.00                            | 20.60                              |
| 31680     | 31680                  | 0.00                            | 14.26                              |
| 32934     | 32934                  | 0.00                            | 29.10                              |
| 33645     | 33645                  | 0.00                            | 17.31                              |

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 2.4-2021-02

Validated substance/substance group **Tea tree oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30959-2021-06-11  
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/substance group | 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 54 961 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.
- 24 565 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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 | 28348-119841         | 1       |
| Taoasis         | Tea tree oil | 20269-117745G09      | 1       |
| Taoasis         | Tea tree oil | 28348-121515         | 1       |
| Taoasis         | Tea tree oil | 28348-121597         | 2       |
| Taoasis         | Tea tree oil | 52642-124559         | 1       |
| Taoasis         | Tea tree oil | 52642-12078          | 1       |
| Taoasis         | Tea tree oil | 52642-124919         | 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       |

- 9253 spectra from 772 *Apo-Ident* customers from a total of 3652 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              | 24 565        |
| Type B | 0              | 120           | 0              | 20 841        |
| Type C | 0              | 42            | 0              | 9253          |

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 % (> 99.9605 %) | 100.0000 % (> 95.7143 %) |
| Type B | 100.0000 % (> 99.9455 %) | 100.0000 % (> 95.0000 %) |
| Type C | 100.0000 % (> 98.7994 %) | 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    | 19.86                  | –                              |
| Carrot seed oil | 44.93                  | –                              |

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                         | 51.84                           |
| 31134     | 31134               | 0.00                         | 53.98                           |
| 31762     | 31762               | 0.00                         | 59.25                           |

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 2.4-2021-02

Validated substance/substance group **Thuja oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33828-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 921 spectra from a total of 450 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 40            | 0              | 20 921        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|---------------------|---------------------------|-----------------------------------|
| Cumin oil           | 45.96                     | —                                 |
| Common wormwood oil | 63.88                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 33828     | 33828                  | 0.00                            | 44.69                              |
| 34287     | 34287                  | 0.00                            | 47.84                              |

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 2.4-2021-02

Validated substance/substance group **Thyme oil, red**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30929-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 504 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20921 spectra from a total of 450 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 | 9434-115525  | 1       |
| Taoasis              | Thyme oil, red | 14381-117385 | 1       |
| Taoasis              | Thyme oil, red | 25394-118296 | 1       |
| Taoasis              | Thyme oil, red | 32444-118785 | 4       |
| Taoasis              | Thyme oil, red | 33635-120088 | 1       |
| Taoasis              | Thyme oil, red | 40517-121881 | 2       |
| Taoasis              | Thyme oil, red | 43637-122713 | 1       |
| Taoasis              | Thyme oil, red | 43637-123574 | 1       |
| Taoasis              | Thyme oil, red | 43637-122852 | 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 | 1976-5867    | 2       |
| Taoasis              | Thyme oil, red | 1976-3100    | 2       |
| Taoasis              | Thyme oil, red | 1976-3455    | 1       |
| Taoasis              | Thyme oil, red | 1976-6717    | 1       |
| Taoasis              | Thyme oil, red | 1976-5865    | 1       |
| Taoasis/Sanacorp     | Thyme oil, red | 1976-3455    | 1       |

- 9269 spectra from 772 *Apo-Ident* customers from a total of 3656 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              | 24 505        |
| Type B | 0              | 40            | 0              | 20 921        |
| Type C | 0              | 21            | 5              | 9269          |

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 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| Type B | 100.0000 % (> 99.9460 %) | 100.0000 % (> 85.0000 %) |
| Type C | 100.0000 % (> 98.8004 %) | 80.7692 % (> 69.2308 %)  |

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

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

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

### Nearest chemometric neighbours

The following table lists the closest chemometric neighbours of the substance/substance group *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 | 19.38                  | —                              |
| 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                         | 26.44                           |
| 31259     | 31259               | 0.00                         | 21.62                           |
| 32482     | 32482               | 0.00                         | 33.30                           |
| 32981     | 32981               | 0.00                         | 24.84                           |
| 34103     | 34103               | 0.00                         | 28.06                           |

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 2.4-2021-02

Validated substance/substance group **Thyme oil, white / Coriander oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31552-2021-06-11  
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/substance group        | Type A | Type B | Type C |
|----------------------------------|--------|--------|--------|
| Thyme oil, white / Coriander oil | 7      | 5      | 9      |

## 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 54 961 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.
- 24 385 spectra from a total of 502 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 761 spectra from a total of 446 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       |

- 9286 spectra from 771 *Apo-Ident* customers from a total of 3666 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 320           | 0              | 24 385        |
| <b>Type B</b> | 0              | 200           | 0              | 20 761        |
| <b>Type C</b> | 0              | 9             | 0              | 9286          |

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 % (> 99.9602 %) | 100.0000 % (> 98.1250 %) |
| Type B | 100.0000 % (> 99.9454 %) | 100.0000 % (> 97.0000 %) |
| Type C | 100.0000 % (> 98.8051 %) | 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 | 20.06                  | –                              |
| Rosewood oil             | 46.29                  | –                              |
| Carrot seed oil          | 53.07                  | –                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31552     | 31552               | 0.00                         | 56.65                           |
| 31690     | 31690               | 0.00                         | 68.88                           |
| 32792     | 32792               | 0.00                         | 58.93                           |
| 33796     | 33796               | 0.00                         | 37.36                           |
| 33818     | 33818               | 0.00                         | 60.07                           |
| 34176     | 34176               | 0.00                         | 40.00                           |
| 34286     | 34286               | 0.00                         | 55.41                           |

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 2.4-2021-02

Validated substance/substance group **Vetiver bourbon oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31546-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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 | 7141-122195 | 2       |
| Taoasis  | Vetiver bourbon oil | 7141-124600 | 2       |
| Taoasis  | Vetiver bourbon oil | 7141-119174 | 1       |
| Taoasis  | Vetiver bourbon oil | 7141-123924 | 1       |
| Taoasis  | Vetiver bourbon oil | 108-232     | 1       |
| Taoasis  | Vetiver bourbon oil | 2060-1665   | 2       |
| Taoasis  | Vetiver bourbon oil | 7141-137885 | 1       |
| Taoasis  | Vetiver bourbon oil | 2060-5667   | 4       |
| Taoasis  | Vetiver bourbon oil | 2060-3449   | 1       |

- 9280 spectra from 772 *Apo-Ident* customers from a total of 3666 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 15            | 0              | 9280          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8022 %) | 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                  | 28.73                  | —                              |
| Myrtle oil                 | 29.49                  | —                              |
| Immortelle oil             | 30.73                  | —                              |
| Manuka oil                 | 34.09                  | —                              |
| Patchouli oil              | 35.01                  | —                              |
| Rose-geranium oil, organic | 35.44                  | —                              |
| Carrot seed oil            | 38.35                  | —                              |
| Lemon grass oil            | 39.01                  | —                              |
| Ginger oil                 | 39.44                  | —                              |
| Hyssop oil                 | 42.65                  | —                              |
| Marjoram oil               | 44.94                  | —                              |
| Tea tree oil               | 47.73                  | —                              |
| Cypress oil                | 52.57                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31546     | 31546               | 0.00                         | 32.92                           |
| 31684     | 31684               | 0.00                         | 31.55                           |
| 33647     | 33647               | 0.00                         | 31.61                           |
| 35143     | 35143               | 0.00                         | 35.01                           |

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

substances of the substance class, even if a second-stage dissolves a subgroup of similar substances, thereby increasing the distances between them. The samples confirmed by NIR support the statistical variance of the original reference substance, but cannot add new aspects or forms of the substance.





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Wart ointment InfectoPharm<sup>®</sup> (NRF 11.31)**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30730-2021-06-11  
Executing company HiperScan GmbH  
Weißeritzstraße 3  
01067 Dresden  
Germany

### Relevant substance names

Wart ointment InfectoPharm<sup>®</sup> (NRF 11.31)

### Special notes

When selecting the *Wart ointment InfectoPharm<sup>®</sup> (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/substance group                           | Type A | Type B | Type C |
|-----------------------------------------------------|--------|--------|--------|
| Wart ointment InfectoPharm <sup>®</sup> (NRF 11.31) | 3      | 3      | 44     |

## 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 |
| Infectopharm | Wart ointment In... | S112001.1 | 35259     | 40      | not required |

## Validation samples

A total of 54 961 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 *Wart ointment InfectoPharm®* (NRF 11.31). These samples are listed above in the [calibration samples](#) section. The reference samples come from 3 different batches.
- 24 545 spectra from a total of 506 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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 <sup>®</sup> ... | S021601.1 | 32593     | 40      |
| Infectopharm | Wart ointment InfectoPharm <sup>®</sup> ... | S071602.1 | 32953     | 40      |
| Infectopharm | Wart ointment InfectoPharm <sup>®</sup> ... | S061801.1 | 34517     | 40      |
| Infectopharm | Wart ointment InfectoPharm <sup>®</sup> ... | S071602.1 | 33515     | 40      |

- 20 801 spectra from a total of 448 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.

- 243 spectra from 104 *Apo-Ident* customers from 56 batches from the substance/substance group *Wart ointment InfectoPharm<sup>®</sup> (NRF 11.31)*.
- Among them are spectra of independent samples from 15 batches from which no spectra have been included in the database structure. These are sorted upwards in the following table.

| Supplier                   | Substance                                   | Batch       | Spectra |
|----------------------------|---------------------------------------------|-------------|---------|
| Caelo                      | Wart ointment InfectoPharm <sup>®</sup> ... | S111202     | 1       |
| Caelo                      | Wart ointment InfectoPharm <sup>®</sup> ... | s0617012    | 1       |
| Caelo                      | Wart ointment InfectoPharm <sup>®</sup> ... | S0215011    | 3       |
| infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... | S0211604    | 1       |
| Infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... | S041301     | 1       |
| Infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... | 3013I-07003 | 1       |
| Infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... | S111202     | 1       |
| InfectoPharm               | Wart ointment InfectoPharm <sup>®</sup> ... | S0215011    | 1       |
| InfectoPharm               | Wart ointment InfectoPharm <sup>®</sup> ... | s061801     | 1       |
| Infectopharm / Phönix      | Wart ointment InfectoPharm <sup>®</sup> ... | 4117A-03898 | 1       |
| Infectopharm / Phönix      | Wart ointment InfectoPharm <sup>®</sup> ... | 3718A-03898 | 1       |
| Infectopharm GmbH          | Wart ointment InfectoPharm <sup>®</sup> ... | s061801-1   | 1       |
| Infectopharm Sanacorp      | Wart ointment InfectoPharm <sup>®</sup> ... | S061801     | 1       |
| Infectopharm/AHD           | Wart ointment InfectoPharm <sup>®</sup> ... | S1219021    | 1       |
| InfectoPharm/Anzag         | Wart ointment InfectoPharm <sup>®</sup> ... | 716A-03898  | 1       |
| Infectopharm/Noweda        | Wart ointment InfectoPharm <sup>®</sup> ... | S0716021    | 1       |
| Infectopharm/Römer/Noweda  | Wart ointment InfectoPharm <sup>®</sup> ... | S0215011    | 2       |
| Infectopharm/Spangro       | Wart ointment InfectoPharm <sup>®</sup> ... | S061801-1   | 1       |
| Löwen City-Apotheke Bar... | Wart ointment InfectoPharm <sup>®</sup> ... | 8032013     | 1       |
| Phönix, Infectopharm,03... | Wart ointment InfectoPharm <sup>®</sup> ... | S129021     | 1       |
| AHD                        | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Caelo                      | Wart ointment InfectoPharm <sup>®</sup> ... |             | 3       |
| Eigenherstellung           | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Euro OTC                   | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Fagron                     | Wart ointment InfectoPharm <sup>®</sup> ... |             | 4       |
| Gehe                       | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| GEHE                       | Wart ointment InfectoPharm <sup>®</sup> ... |             | 3       |
| gehe/infecto               | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Ichthyol-Gesellschaft C... | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Infec/ Phönix              | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Infect/PX                  | Wart ointment InfectoPharm <sup>®</sup> ... |             | 2       |
| infectipharm/Phönix        | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |
| Infecto Pharm / Noweda     | Wart ointment InfectoPharm <sup>®</sup> ... |             | 4       |
| Infecto/Gehe               | Wart ointment InfectoPharm <sup>®</sup> ... |             | 1       |

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| Supplier                   | Substance                                   | Batch | Spectra |
|----------------------------|---------------------------------------------|-------|---------|
| Infecto/Spangro            | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectoph./Gehe            | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectoph./Kehr            | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... |       | 3       |
| Infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... |       | 53      |
| InfectoPharm               | Wart ointment InfectoPharm <sup>®</sup> ... |       | 14      |
| Infectopharm (Phoenix)     | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm / Alliance    | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm / Alliance... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm / Alliance... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| Infectopharm / Gehe        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 3       |
| InfectoPharm / Gehe        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm / Phoenix     | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm / Phönix      | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm / Sanacorp    | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm Arzneimittel  | Wart ointment InfectoPharm <sup>®</sup> ... |       | 10      |
| Infectopharm Arzneimitt... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| INFECTOPHARM -Noweda       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/              | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/ Alliance     | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/ E            | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/ Noweda       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 3       |
| InfectoPharm/ Phoenix/ ... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| Infectopharm/ Sanacorp     | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/AHD           | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Alliance H... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/AllianceHe... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Allianz       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 4       |
| Infectopharm/Anzag         | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| InfectoPharm/Anzag         | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| Infectopharm/Ebert         | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/Fiebig        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/G             | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Gehe          | Wart ointment InfectoPharm <sup>®</sup> ... |       | 13      |
| Infectopharm/GEHE          | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/Gehe          | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/GEHE          | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| INFECTOPHARM/GEHE 02.05... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| INFECTOPHARM/GEHE 07.07... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| INFECTOPHARM/GEHE 28.09... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/K             | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Kehr          | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharm/Krieger       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Noweda        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 12      |
| InfectoPharm/Noweda        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 3       |
| Infectopharm/Phoenix       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| InfectoPharm/Phoenix       | Wart ointment InfectoPharm <sup>®</sup> ... |       | 6       |
| Infectopharm/Phoenix Le... | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm/Phönix        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 7       |
| InfectoPharm/Phönix        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectoPharma              | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| InfectopharmNoweda         | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Infectopharm               | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| nfectoPharm                | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Noweda                     | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Noweda/Infecto Pharma      | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Noweda/infectopharm        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |
| Noweda/Infectopharm        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 2       |
| Noweda/InfectoPharm        | Wart ointment InfectoPharm <sup>®</sup> ... |       | 6       |
| Phönix Gotha               | Wart ointment InfectoPharm <sup>®</sup> ... |       | 1       |

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| Supplier                   | Substance                       | Batch | Spectra |
|----------------------------|---------------------------------|-------|---------|
| Phönix/ Infectopharm       | Wart ointment InfectoPharm® ... |       | 1       |
| Phönix/InfectoPharm/ 15... | Wart ointment InfectoPharm® ... |       | 1       |
| Sanacorp                   | Wart ointment InfectoPharm® ... |       | 2       |
| Sanacorp/Infectopharm      | Wart ointment InfectoPharm® ... |       | 1       |

- 9052 spectra from 763 *Apo-Ident* customers from a total of 3620 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 160           | 0              | 24 545        |
| <b>Type B</b> | 0              | 160           | 0              | 20 801        |
| <b>Type C</b> | 0              | 243           | 0              | 9052          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 96.2500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 100.0000 % (> 96.2500 %) |
| <b>Type C</b> | 100.0000 % (> 98.7982 %) | 100.0000 % (> 97.5309 %) |

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

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

Where the number of spectra does 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<br>main model | Distance in<br>second-stage model |
|------------------------------|---------------------------|-----------------------------------|
| Salicylic white paraffin 10% | 129.45                    | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 30730     | 30730                  | 0.00                            | 221.36                             |
| 30905     | 30905                  | 0.00                            | 220.21                             |
| 30906     | 30906                  | 0.00                            | 218.91                             |
| 35259     | 35259                  | 0.00                            | 203.48                             |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Water and aqueous solutions</b>                              |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 31047-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group   | Type A | Type B | Type C |
|-----------------------------|--------|--------|--------|
| Water and aqueous solutions | 25     | 44     | 252    |



## 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 <sup>®</sup> solut... | KP08DR1   | 31047     | 40      | not required |
| Bayer            | Bepanthen <sup>®</sup> solut... | KP0ASHC   | 31857     | 60      | not required |
| Bayer            | Bepanthen <sup>®</sup> 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 <sup>®</sup> SF pH4... | 1503D017  | 31671     | 60      | not required |
| Fagron           | SyrSpend <sup>®</sup> SF pH4... | 1503D017  | 31723     | 60      | not required |
| Fagron           | SyrSpend <sup>®</sup> SF pH4... | 1704492/1 | 33787     | 40      | not required |
| Fagron           | SyrSpend <sup>®</sup> SF pH4... | 1503D009  | 31670     | 60      | not required |
| Fagron           | SyrSpend <sup>®</sup> SF pH4... | 1412D002  | 31722     | 60      | not required |
| Fagron           | SyrSpend <sup>®</sup> 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*    |
| Caelo            | Water                           | 20003298  | 35239     | 40      | 20201113*    |
| Caelo            | Water                           | 20003299  | 35240     | 40      | 20201113*    |
| Caelo            | Water                           | 20003301  | 35242     | 40      | 20201113*    |
| Hedinger         | Water                           | 219066    | 31623     | 60      | not required |

## Validation samples

A total of 54 961 spectra were provided for validation. The results were evaluated separately according to the following sample categories:

**Type A** All calibration spectra.

- 1285 spectra of 27 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 25 different batches.
- 23 420 spectra from a total of 484 batches from further 154 substances. These spectra were recorded by *HiperScan GmbH*. *Type A* samples are documented within this entire report. If the

\*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.



substance can be identified with this [chemometric model](#), the samples are listed in the *Type A* section of each substance page. If the substance cannot be identified by this model, the samples are listed in [Appendix A](#). The samples in [Appendix A](#) were added for model generation not with the intention to have the model identify these substances, but with the intention to make the model reject them despite their similarity to substances identifiable.

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

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

- 1805 spectra of 46 reference samples from the substance/substance group *Water and aqueous solutions*.
- Among them are spectra of independent samples from 44 batches from which no spectra have been included in the database 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 <sup>®</sup> solution           | KP0B60L   | 32719     | 40      |
| Bayer            | Bepanthen <sup>®</sup> solution           | KP0BJ61   | 32949     | 40      |
| Retterspitz GmbH | Retterspitz external                      | 016179    | 32784     | 30      |
| Retterspitz GmbH | Retterspitz external                      | 017192    | 34049     | 40      |
| Fagron           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1503255   | 32738     | 40      |
| Fagron           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1603252/2 | 32842     | 40      |
| Fagron           | SyrSpend <sup>®</sup> 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      |
| 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      |

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| Supplier | Substance                               | Batch    | Sample ID          | Spectra |
|----------|-----------------------------------------|----------|--------------------|---------|
| Caelo    | Water                                   | 182286   | 34243              | 40      |
| Caelo    | Water                                   | 181952   | 34244              | 40      |
| Caelo    | Water                                   | 192421   | 34765              | 40      |
| Caelo    | Water                                   | 20002402 | 35114              | 40      |
| Caelo    | Water                                   | 20002910 | 35237              | 40      |
| Caelo    | Water                                   | 20002911 | 35238              | 40      |
| Caelo    | Water                                   | 20003300 | 35241              | 40      |
| Caelo    | Water                                   | 20003876 | 35243              | 40      |
| Fagron   | SyrSpend <sup>®</sup> SF pH4 aroma free | 1704493  | 33631              | 40      |
| Caelo    | Water                                   | 15068701 | 31675 <sup>†</sup> | 15      |

- 19156 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.

- 927 spectra from 253 *Apo-Ident* customers from 258 batches from the substance/substance group *Water and aqueous solutions*.
- Among them are spectra of independent samples from 250 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            | 2       |
| Caelo                | Aloe Vera gel, 1:1                        | 18194304            | 3       |
| 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       |
| 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            | 2       |
| Caelo                | Aloe vera gel, 10x concentra...           | 15185512            | 1       |
| Caesar & Loretz GmbH | Aloe vera gel, 10x concentra...           | 18125504            | 1       |
| Spinnrad             | Aloe vera gel, 10x concentra...           | 319502021           | 1       |
| Fischar              | Bepanthen <sup>®</sup> solution           | 6317104             | 1       |
| Liechtenstein        | Bepanthen <sup>®</sup> solution           | 2300380R            | 1       |
| Retterspitz/ Phoenix | Retterspitz external                      | 17224               | 1       |
| Retterspitz/ Phoenix | Retterspitz external                      | 18045               | 1       |
| apomix               | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1800673/1           | 1       |
| Apomix/ Sanacorp     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 15C19/C             | 1       |
| Bombastus            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2           | 1       |
| Caelo                | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1712024             | 1       |
| Caelo                | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1900093P-190927-2   | 1       |
| Caelo                | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2P-190927-3 | 1       |
| Caelo                | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1507318             | 3       |

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<sup>†</sup>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 <sup>®</sup> SF pH4 cherry aroma | 1800673/1           | 2       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1707302/1           | 2       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909673             | 2       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1702015             | 4       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2           | 1       |
| Euro OTC        | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1704492/01          | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 15C19/C             | 7       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1507318             | 5       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1503255             | 19      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1603252/2           | 11      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1612631             | 22      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1701543/3           | 5       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1707302/1           | 7       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1702015(2Flaschen)  | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 2x1712024           | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1800673/2           | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2           | 32      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2P-190618-2 | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 2000326             | 2       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20004221            | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1802928             | 5       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909673             | 32      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 720023-0003         | 2       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1908041             | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20007317            | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20007125            | 3       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1800673/1P-180827-1 | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2P-180922-1 | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2P-190808-3 | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20000326P-200709-3  | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 518E-07041          | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20004332            | 4       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909423/1           | 7       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1707032/1           | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1712017             | 5       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20000326            | 25      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20006936            | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 4415A-07041         | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909423-2           | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1712024             | 21      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 18062331            | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1800673             | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/1           | 4       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 18000673/1          | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1704992/1           | 1       |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2           | 34      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1900093             | 19      |
| Fagron          | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 180067/1            | 1       |
| Fargon/AHD      | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2           | 1       |
| Fragron         | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1702015             | 1       |
| Gehe            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2           | 1       |
| Gehe            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909673             | 1       |
| Gehe            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 17122017            | 1       |
| GEHE            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1712024             | 1       |
| GEHE            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1803724/2           | 3       |
| GEHE            | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1806233/2           | 2       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1704492             | 1       |
| Ichthyol/Gehe   | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1900093             | 1       |
| Kehr.21.07.2020 | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20000326            | 1       |
| Caelo           | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1503255             | 1       |

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| Supplier                   | Substance                                 | Batch       | Spectra |
|----------------------------|-------------------------------------------|-------------|---------|
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1702015     | 24      |
| PHÖNIX                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1704492/1   | 1       |
| Phönix Gotha               | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1909673     | 1       |
| Phönix Gotha               | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20000326    | 2       |
| Phönix, Caesar&Loretz G... | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 20004332    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 19094223/2  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1800673/1   | 20      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 180623312   | 1       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1704493     | 1       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1812018     | 1       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712023/2   | 3       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712018     | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1410D020    | 7       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 15C12/E     | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1609686     | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 15C12E      | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1706769/1   | 7       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1706769     | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712018     | 8       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 27121704    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712023/1   | 9       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712023/2   | 23      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 18026531    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 102653/1    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1802653/4   | 2       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1804245/1   | 24      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 17122018    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 18025653/1  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1812150/2   | 11      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1911010     | 3       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1907122     | 7       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 190114110   | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1704493     | 11      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1802653/1   | 17      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/2B  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/2A  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 518E-07040  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 22092008    | 2       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 22092007    | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/2   | 48      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712023/02  | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 4415A-07040 | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/1   | 3       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1814231     | 20      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 720024-0003 | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1802653/2   | 5       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1802654     | 7       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 18c2653/1   | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 20004219    | 2       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1906126     | 14      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1804245/2   | 2       |
| Fargron/PNACH              | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1712023/1   | 1       |
| Fgron / Kehr 03.02.2020    | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1812150/2   | 1       |
| Gehe                       | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/2   | 5       |
| Gehe                       | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1812150/2   | 2       |
| Gehe                       | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1814231     | 3       |
| Herkel B.V./Kehr           | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1808206/2   | 1       |
| Kehr.26.03.2020            | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1814231     | 1       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 19011410    | 2       |
| Caelo                      | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1906126     | 2       |

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| Supplier                   | Substance                               | Batch            | Spectra |
|----------------------------|-----------------------------------------|------------------|---------|
| Noweda                     | SyrSpend <sup>®</sup> SF pH4 aroma free | 1712023/2        | 1       |
| Phoenix                    | SyrSpend <sup>®</sup> SF pH4 aroma free | 1804245/1        | 8       |
| Phönix                     | SyrSpend <sup>®</sup> SF pH4 aroma free | 1802653/1        | 1       |
| Phönix                     | SyrSpend <sup>®</sup> SF pH4 aroma free | 1802653/01       | 1       |
| Phönix Gotha               | SyrSpend <sup>®</sup> SF pH4 aroma free | 1802653/1        | 2       |
| Phönix Gotha               | SyrSpend <sup>®</sup> SF pH4 aroma free | 1802654          | 4       |
| Phönix/Fagro GmbH&Co.KG... | SyrSpend <sup>®</sup> SF pH4 aroma free | 20004219         | 1       |
| Sanacorp                   | SyrSpend <sup>®</sup> SF pH4 aroma free | 19011410         | 1       |
| Tiofarma B.V.              | SyrSpend <sup>®</sup> SF pH4 aroma free | 1410D020         | 1       |
| Caelo                      | Water                                   | 17145001         | 3       |
| apomix/ Fiebig             | Water                                   | 17H24-T09-044709 | 1       |
| Apotheke                   | Water                                   | 4/20             | 1       |
| 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                                   | L0TAP0041        | 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                                   | 17282701         | 3       |
| Caelo                      | Water                                   | 17277102         | 2       |
| Caelo                      | Water                                   | 18042901         | 1       |
| Caelo                      | Water                                   | 18093501         | 3       |
| Caelo                      | Water                                   | 17295701         | 1       |
| Caelo                      | Water                                   | 18109501         | 1       |
| Caelo                      | Water                                   | 219181           | 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                                   | L0TAP-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                                   | L0TAP0078        | 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                                   | 18305301         | 1       |
| 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       |

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| Supplier                   | Substance | Batch            | Spectra |
|----------------------------|-----------|------------------|---------|
| 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       |
| 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 | 2       |
| 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-T09-047709 | 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 | 3       |
| Fagron                     | Water     | 15H25-T14-025670 | 1       |
| Fagron                     | Water     | 16K25-C20-17409  | 1       |
| Fagron                     | Water     | 16L12-T16-039628 | 1       |
| Fagron                     | Water     | 18G16-T01-058118 | 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       |
| Euro OTC                   | Water     | 15F24-T01-023879 | 1       |
| Fresenius /Noweda          | Water     | 19KK24GA         | 1       |
| Gehe                       | Water     | 17219101         | 1       |

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| Supplier                   | Substance                                 | Batch            | Spectra |
|----------------------------|-------------------------------------------|------------------|---------|
| 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       |
| 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       |
| Wepa/Wepa/ 13.05.2019/ ... | Water                                     | LOTAP0101        | 1       |
| Caelo                      | Aloe vera gel, 10x concentra...           | 15185503         | 1       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1503D017         | 2       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 cherry aroma | 1704492/1        | 9       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1412D002         | 3       |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 19011410         | 18      |
| Fagron                     | SyrSpend <sup>®</sup> SF pH4 aroma free   | 1503D009         | 3       |
| Caelo                      | Water                                     |                  | 1       |
| kerndl-Noweda              | Water                                     |                  | 2       |
| Serumwerk Bernburg         | Water                                     |                  | 1       |
| serumwerk bernburg - Gehe  | Water                                     |                  | 5       |

- 8368 spectra from 741 *Apo-Ident* customers from a total of 3418 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              | 1285          | 0              | 23 420        |
| Type B | 0              | 1803          | 2              | 19 016        |
| Type C | 0              | 912           | 15             | 8356          |

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 % (> 99.9601 %) | 100.0000 % (> 99.5331 %) |
| Type B | 100.0000 % (> 99.9455 %) | 99.8892 % (> 99.7230 %)  |
| Type C | 100.0000 % (> 98.7890 %) | 98.3819 % (> 98.0583 %)  |

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

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

Where the number of spectra does 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                      | 14.48                  | —                              |
| Sebexol® cream lotion pH 5         | 26.88                  | —                              |
| Sebexol® basic pH 5 formula basis  | 27.75                  | —                              |
| Wofacutan wash lotion              | 32.21                  | —                              |
| Hans Karrer Hydrocream MicroSilver | 34.49                  | —                              |
| Dimeticone ointment 10% SR         | 35.16                  | —                              |
| Excipial® U Hydrolotio             | 40.34                  | —                              |
| Abitima® clinic face cream         | 46.56                  | —                              |
| Hans Karrer Lipolotion MicroSilver | 65.48                  | —                              |

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 |
|-----------|---------------------|------------------------------|---------------------------------|
| 31047     | 31047               | 0.00                         | 26.97                           |
| 31145     | 31145               | 0.00                         | 31.17                           |
| 31146     | 31146               | 0.00                         | 29.76                           |
| 31623     | 31623               | 0.00                         | 31.55                           |
| 31670     | 31670               | 0.00                         | 31.17                           |
| 31671     | 31671               | 0.00                         | 31.59                           |
| 31675     | 31675               | 0.00                         | 33.90                           |
| 31722     | 31722               | 0.00                         | 29.96                           |
| 31723     | 31723               | 0.00                         | 30.08                           |
| 31857     | 31857               | 0.00                         | 26.79                           |
| 31862     | 31862               | 0.00                         | 30.07                           |
| 31866     | 31866               | 0.00                         | 32.73                           |
| 31880     | 31880               | 0.00                         | 33.91                           |
| 31881     | 31881               | 0.00                         | 32.55                           |
| 32079     | 32079               | 0.00                         | 32.87                           |
| 32313     | 32313               | 0.00                         | 29.13                           |
| 32785     | 32785               | 0.00                         | 19.05                           |
| 33430     | 33430               | 0.00                         | 25.18                           |
| 33431     | 33431               | 0.00                         | 25.45                           |
| 33612     | 33612               | 0.00                         | 26.37                           |
| 33787     | 33787               | 0.00                         | 29.64                           |
| 34767     | 34767               | 0.00                         | 32.52                           |
| 35049     | 35049               | 0.00                         | 26.01                           |
| 35077     | 35077               | 0.00                         | 28.92                           |
| 35239     | 35239               | 0.00                         | 32.05                           |
| 35240     | 35240               | 0.00                         | 31.81                           |
| 35242     | 35242               | 0.00                         | 31.64                           |

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 2.4-2021-02

|                                     |                                                                 |
|-------------------------------------|-----------------------------------------------------------------|
| Validated substance/substance group | <b>Wax ointment (stabilised)</b>                                |
| Substance class                     | APIs & excipients, liquid/semi-solid (other)                    |
| Report date                         | 11/06/2021                                                      |
| Report number                       | 31111-2021-06-11                                                |
| Executing company                   | HiperScan GmbH<br>Weißeritzstraße 3<br>01067 Dresden<br>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/substance group | 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 54 961 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.
- 24 465 spectra from a total of 504 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      |

- 20641 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.

- 498 spectra from 174 *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       |
| Caelo               | Wax ointment (stabilised) | 15424301   | 17      |
| Caelo/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) | 11355201   | 2       |
| Caelo               | Wax ointment (stabilised) | 12352051   | 1       |
| 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) | 14236002   | 3       |
| Caelo               | Wax ointment (stabilised) | 28051511   | 1       |
| Caelo               | Wax ointment (stabilised) | 15205402   | 12      |
| Caelo               | Wax ointment (stabilised) | 15424402   | 4       |
| Caelo               | Wax ointment (stabilised) | 16121502   | 4       |
| Caelo               | Wax ointment (stabilised) | 16121501   | 8       |
| Caelo               | Wax ointment (stabilised) | 16133401   | 19      |

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| Supplier                   | Substance                 | Batch       | Spectra |
|----------------------------|---------------------------|-------------|---------|
| Caelo                      | Wax ointment (stabilised) | 1524401     | 1       |
| Caelo                      | Wax ointment (stabilised) | 17014901    | 27      |
| Caelo                      | Wax ointment (stabilised) | 17015002    | 1       |
| Caelo                      | Wax ointment (stabilised) | 17171401    | 18      |
| Caelo                      | Wax ointment (stabilised) | 17294202    | 16      |
| Caelo                      | Wax ointment (stabilised) | 18034602    | 17      |
| Caelo                      | Wax ointment (stabilised) | 18034601    | 3       |
| Caelo                      | Wax ointment (stabilised) | 19040001    | 8       |
| Caelo                      | Wax ointment (stabilised) | 19040002    | 13      |
| 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 | 3       |
| Caelo                      | Wax ointment (stabilised) | 15424401    | 7       |
| Caelo                      | Wax ointment (stabilised) | 17015001    | 20      |
| Caelo                      | Wax ointment (stabilised) | 1524301     | 1       |
| Caelo                      | Wax ointment (stabilised) | 19000783001 | 12      |
| 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) | 18258501    | 21      |
| Caelo                      | Wax ointment (stabilised) | 19190501    | 15      |
| Caelo                      | Wax ointment (stabilised) | 13159303    | 2       |
| Caelo                      | Wax ointment (stabilised) | 11321302    | 1       |
| Caerol/Noweda              | Wax ointment (stabilised) | 17294201    | 1       |
| Caerol/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/Je... | 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    | 11      |
| Hedinger GmbH & Co KG      | Wax ointment (stabilised) | 18034602    | 1       |
| Henry Lamotte Olis GmbH... | Wax ointment (stabilised) | 15424301    | 1       |
| Noweda                     | Wax ointment (stabilised) | 17171401    | 1       |

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| Supplier                  | Substance                 | Batch    | Spectra |
|---------------------------|---------------------------|----------|---------|
| Caelo                     | Wax ointment (stabilised) | 13307802 | 13      |
| 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      |

- 8797 spectra from 759 *Apo-Ident* customers from a total of 3612 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              | 24 465        |
| Type B | 0              | 320           | 0              | 20 641        |
| Type C | 0              | 495           | 3              | 8797          |

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 % (> 99.9603 %) | 100.0000 % (> 97.5000 %) |
| Type B | 100.0000 % (> 99.9453 %) | 100.0000 % (> 98.1250 %) |
| Type C | 100.0000 % (> 98.7980 %) | 99.3976 % (> 98.7952 %)  |

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

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

Where the number of spectra does 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<br>main model | Distance in<br>second-stage model |
|---------------------------------------------------|---------------------------|-----------------------------------|
| Cottonwood ointment                               | 26.01                     | —                                 |
| Neribas <sup>®</sup> fat ointment                 | 26.49                     | —                                 |
| Marjoram ointment                                 | 27.26                     | —                                 |
| Protegin <sup>®</sup> XN                          | 32.26                     | —                                 |
| Excipial <sup>®</sup> almond oil ointment         | 37.43                     | —                                 |
| Balm Bio Nature                                   | 37.62                     | —                                 |
| Salicylic white paraffin 10%                      | 42.48                     | —                                 |
| White paraffin oil                                | 43.46                     | —                                 |
| Argan oil                                         | 44.43                     | —                                 |
| Deumavan <sup>®</sup> protection ointment neutral | 62.56                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31111     | 31111                  | 0.00                            | 36.28                              |
| 31167     | 31167                  | 0.00                            | 38.78                              |
| 31444     | 31444                  | 0.00                            | 35.68                              |
| 31911     | 31911                  | 0.00                            | 31.96                              |
| 31912     | 31912                  | 0.00                            | 39.22                              |

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 2.4-2021-02

Validated substance/substance group **White paraffin oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 32342-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 450 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       |

- 9287 spectra from 771 *Apo-Ident* customers from a total of 3669 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 80            | 0              | 20 881        |
| <b>Type C</b> | 0              | 8             | 0              | 9287          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 100.0000 % (> 92.5000 %) |
| <b>Type C</b> | 100.0000 % (> 98.8060 %) | 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.

| <b>Substance</b>                                  | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|---------------------------------------------------|-------------------------------|---------------------------------------|
| Deumavan <sup>®</sup> protection ointment neutral | 13.32                         | —                                     |
| Neribas <sup>®</sup> fat ointment                 | 21.39                         | —                                     |
| Cottonwood ointment                               | 24.49                         | —                                     |
| Marjoram ointment                                 | 25.69                         | —                                     |
| Protegin <sup>®</sup> XN                          | 25.79                         | —                                     |
| Asche Basis <sup>®</sup> fat ointment             | 27.73                         | —                                     |
| Wax ointment (stabilised)                         | 43.85                         | —                                     |
| Lygal <sup>®</sup> head ointment N 3%             | 43.95                         | —                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 32342            | 32342                      | 0.00                                | 14.96                                  |
| 32565            | 32565                      | 0.00                                | 17.16                                  |

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

variance of the original reference substance, but cannot add new aspects or forms of the substance.





# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Wintergreen oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 30455-2021-06-11  
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/substance group | 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 54 961 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.
- 24 609 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 801 spectra from a total of 448 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 | 10318714     | 1       |
| Caelo           | Wintergreen oil | 15087406     | 1       |
| Caelo           | Wintergreen oil | 10318703     | 1       |
| Caelo           | Wintergreen oil | 13099205     | 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       |

- 9284 spectra from 772 *Apo-Ident* customers from a total of 3664 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 96            | 0              | 24 609        |
| <b>Type B</b> | 0              | 159           | 1              | 20 801        |
| <b>Type C</b> | 0              | 10            | 1              | 9284          |

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:

|               | <b>Specificity</b>       | <b>Recognition rate</b>  |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9607 %) | 100.0000 % (> 93.7500 %) |
| <b>Type B</b> | 100.0000 % (> 99.9454 %) | 99.3750 % (> 97.5000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8038 %) | 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.

| <b>Substance</b> | <b>Distance in main model</b> | <b>Distance in second-stage model</b> |
|------------------|-------------------------------|---------------------------------------|
| Clove oil        | 273.51                        | —                                     |

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:

| <b>Sample ID</b> | <b>Reference sample ID</b> | <b>Distance to reference sample</b> | <b>Distance to next foreign sample</b> |
|------------------|----------------------------|-------------------------------------|----------------------------------------|
| 31543            | 31543                      | 0.00                                | 293.11                                 |
| 32807            | 32807                      | 0.00                                | 294.10                                 |

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

# VALIDATION REPORT

## IdentModule 2.4-2021-02

Validated substance/substance group **Yarrow oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 33795-2021-06-11  
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/substance group | 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 54 961 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.
- 24 625 spectra from a total of 507 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 841 spectra from a total of 448 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 80            | 0              | 24 625        |
| <b>Type B</b> | 0              | 108           | 12             | 20 841        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9608 %) | 100.0000 % (> 92.5000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9455 %) | 90.0000 % (> 87.5000 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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                | 20.65                  | —                              |
| Myrtle oil               | 21.77                  | —                              |
| Hyssop oil               | 24.81                  | —                              |
| Marjoram oil             | 27.64                  | —                              |
| Angelica root oil        | 33.68                  | —                              |
| Spearmint oil            | 41.65                  | —                              |
| Ravensara oil            | 42.04                  | —                              |
| Juniper oil              | 43.57                  | —                              |
| Cypress oil              | 46.56                  | —                              |
| Dwarf pine oil           | 46.94                  | —                              |
| Sage oil                 | 49.23                  | —                              |
| Matricaria oil, morrocan | 49.37                  | —                              |
| Niaouli oil              | 49.89                  | —                              |
| Cumin oil                | 50.89                  | —                              |

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                         | 52.12                           |
| 33822     | 33822               | 0.00                         | 21.05                           |

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 2.4-2021-02

Validated substance/substance group **Ylang-ylang oil**  
Substance class APIs & excipients, liquid/semi-solid (other)  
Report date 11/06/2021  
Report number 31506-2021-06-11  
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/substance group | 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 54 961 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.
- 24 505 spectra from a total of 505 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 <sup>†</sup>. The following applies to the remaining unmarked samples: In the same batch, there 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      |

- 20 881 spectra from a total of 449 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.
- 9295 spectra from 772 *Apo-Ident* customers from a total of 3675 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 |
|---------------|----------------|---------------|----------------|---------------|
| <b>Type A</b> | 0              | 200           | 0              | 24 505        |
| <b>Type B</b> | 0              | 34            | 46             | 20 881        |
| <b>Type C</b> | 0              | 0             | 0              | 9295          |

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         |
|---------------|--------------------------|--------------------------|
| <b>Type A</b> | 100.0000 % (> 99.9604 %) | 100.0000 % (> 97.0000 %) |
| <b>Type B</b> | 100.0000 % (> 99.9456 %) | 42.5000 % (> 38.7500 %)  |
| <b>Type C</b> | 100.0000 % (> 98.8225 %) | 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<br>main model | Distance in<br>second-stage model |
|----------------|---------------------------|-----------------------------------|
| Clary sage oil | 37.84                     | —                                 |
| Petitgrain oil | 48.59                     | —                                 |
| Lavender oil   | 61.79                     | —                                 |

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<br>sample ID | Distance to<br>reference sample | Distance to<br>next foreign sample |
|-----------|------------------------|---------------------------------|------------------------------------|
| 31506     | 31506                  | 0.00                            | 86.81                              |
| 31653     | 31653                  | 0.00                            | 35.41                              |
| 32808     | 32808                  | 0.00                            | 74.49                              |
| 34382     | 34382                  | 0.00                            | 68.75                              |

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.

## *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 <sup>®</sup> clinic body lotion             | 145054           | 40      | not required |
| Actavis            | Abitima <sup>®</sup> clinic body lotion             | 159997           | 40      | not required |
| Actavis            | Abitima <sup>®</sup> clinic body lotion             | 159997           | 40      | not required |
| Dr. Wolff          | Anefug <sup>®</sup> Simplex                         | 234280           | 40      | not required |
| Dr. Wolff          | Anefug <sup>®</sup> Simplex                         | 237590           | 40      | 1407216      |
| Primavera          | Anise seed oil                                      | 00480L26         | 40      | not required |
| Taoasis            | Black cumin oil                                     | 504511-115611    | 40      | not required |
| Koko               | dermaviduals <sup>®</sup> base gel                  | L003L13          | 60      | not required |
| Allergika          | Dermifant <sup>®</sup> kids lotion                  | 1301020          | 80      | not required |
| Allergika          | Dermifant <sup>®</sup> kids lotion                  | 1306020          | 40      | not required |
| Allergika          | Dermifant <sup>®</sup> kids lotion                  | 1607080          | 40      | not required |
| Allergika          | Dermifant <sup>®</sup> kids lotion                  | 1705081          | 40      | not required |
| Primavera          | Douglas fir oil                                     | 00539M26         | 40      | not required |
| Fagron             | Fitalite <sup>TM</sup>                              | 14B18-T01-010352 | 60      | not required |
| Fagron             | Fitalite <sup>TM</sup>                              | 14B18-T01-010352 | 60      | not required |
| Fagron             | Fitalite <sup>TM</sup>                              | 1503259          | 40      | not required |
| Fagron             | Fitalite <sup>TM</sup>                              | 1503259          | 40      | not required |
| Fagron             | Fitalite <sup>TM</sup>                              | 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 <sup>®</sup> base ointment                  | M031             | 40      | not required |
| Spirig Pharma      | Kerasal <sup>®</sup> 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 <sup>®</sup> acute 0.5%                      | 334620           | 40      | not required |
| Dr. Wolff          | Linola <sup>®</sup> sun protection SPF 50 lotion    | 134530           | 40      | not required |
| Primavera          | Litsea oil                                          | 00496L26         | 40      | not required |
| Caelo              | Milking grease Special without Osmaron <sup>®</sup> | 162049           | 40      | 20160711*    |
| Paddock            | Ora-Blend <sup>®</sup>                              | 2280130          | 40      | not required |
| Perrigo            | Ora-Blend <sup>®</sup> SF                           | 3112578          | 40      | not required |
| Fagron             | Ora-Plus <sup>®</sup>                               | 3334081          | 60      | not required |
| Perrigo            | Ora-Plus <sup>®</sup>                               | 3334081          | 40      | not required |
| Fagron             | Ora-Sweet <sup>®</sup>                              | 3062252          | 40      | not required |
| Perrigo            | Ora-Sweet <sup>®</sup>                              | 3062252          | 40      | not required |
| Stiefel            | Physiogel <sup>®</sup> hypoallergenic cream         | 343P             | 40      | not required |
| Stiefel            | Physiogel <sup>®</sup> hypoallergenic cream         | 6940             | 40      | not required |
| Caelo              | Pine oil rubbing alcohol                            | 162091           | 40      | 20160713*    |
| Stoko              | Praecutan <sup>®</sup> lotion F                     | 0915777806       | 40      | not required |
| Stoko              | Praecutan <sup>®</sup> 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 |

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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 <sup>®</sup> gel      | 401B101               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> gel      | 401B101               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> gel      | 403I143               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> gel      | 403I143               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> gel      | 403I143               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> ointment | 410B113               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> ointment | 410B113               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> ointment | 408C141               | 40      | not required |
| Bene               | Thrombocid <sup>®</sup> 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 <sup>®</sup>            | 33851A                | 40      | not required |
| Hecht Pharma ...   | Ultrabas <sup>®</sup>            | 34069                 | 40      | not required |
| Bayer              | Ultrapril <sup>®</sup>           | 22100A                | 40      | not required |
| Bayer              | Ultrasicc <sup>®</sup>           | 33614A                | 40      | not required |
| Hecht Pharma ...   | Ultrasicc <sup>®</sup>           | 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 <sup>TM</sup>          | 14B19-T02-010391      | 60      | not required |
| Fagron             | Versatile <sup>TM</sup>          | 14B19-T02-010391      | 60      | not required |
| Fagron             | Versatile <sup>TM</sup>          | 1503256               | 40      | not required |
| Fagron             | Versatile <sup>TM</sup>          | 1503256               | 40      | not required |
| Fagron             | Versatile <sup>TM</sup>          | 1503256               | 40      | not required |
| Fagron             | Versatile <sup>TM</sup> Rich     | 14B19-T08-010395      | 60      | not required |
| Fagron             | Versatile <sup>TM</sup> Rich     | 14B19-T04-010395      | 60      | not required |
| Fagron             | Versatile <sup>TM</sup> Rich     | 1503257               | 40      | not required |
| Fagron             | Versatile <sup>TM</sup> Rich     | 1503257               | 40      | not required |
| Fagron             | Versatile <sup>TM</sup> 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 <sup>®</sup> 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 <sup>®</sup> kids lotion   | 1604060              | 1       |
| Sanacorp EK:10,80 ...    | Dermifant <sup>®</sup> kids lotion   | 1705111              | 1       |
| Fagron                   | Fitalite <sup>TM</sup>               | 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%               | 25041301             | 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 <sup>®</sup> base ointment   | S075                 | 1       |
| Galderma/Gehe            | Kerasal <sup>®</sup> base ointment   | S061                 | 1       |
| Galderma/Anzag           | Kerasal <sup>®</sup> base ointment   | S041                 | 4       |
| Spirig                   | Kerasal <sup>®</sup> base ointment   | L0TR012              | 1       |
| Spirig Pharma            | Kerasal <sup>®</sup> base ointment   | N021                 | 1       |
| Spirig/Gehe              | Kerasal <sup>®</sup> base ointment   | S076                 | 1       |
| Spirig/Sanacorp          | Kerasal <sup>®</sup> base ointment   | N011                 | 1       |
| Caelo                    | Milk Cordes <sup>®</sup> O/W Emul... | 13D001               | 2       |
| Ichthyol                 | Milk Cordes <sup>®</sup> O/W Emul... | 60613                | 1       |
| Ichthyol - Gesellschaft  | Milk Cordes <sup>®</sup> O/W Emul... | 11D037               | 1       |
| Ichthyol / Noweda        | Milk Cordes <sup>®</sup> O/W Emul... | 12D008               | 5       |
| IchthyolGmbH/Anzag       | Milk Cordes <sup>®</sup> O/W Emul... | 12D003               | 2       |
| Ichthyol, Noweda         | Milk Cordes <sup>®</sup> O/W Emul... | 13d007               | 1       |
| Fagron                   | Ora-Blend <sup>®</sup> SF            | 3745164              | 1       |
| Fagron                   | Ora-Blend <sup>®</sup> SF            | 4136370              | 1       |
| Gehe                     | Ora-Blend <sup>®</sup> SF            | 2038178              | 1       |
| Gehe                     | Ora-Blend <sup>®</sup> SF            | 3112578              | 1       |
| Perrigo                  | Ora-Blend <sup>®</sup> SF            | 2088609              | 1       |
| Phönix                   | Ora-Blend <sup>®</sup> SF            | 3434856              | 2       |
| Phönix                   | Ora-Blend <sup>®</sup> SF            | 3475164              | 1       |
| Fagron                   | Ora-Sweet <sup>®</sup>               | 3414679              | 1       |
| Fagron                   | Ora-Sweet <sup>®</sup>               | 4247427              | 2       |
| GSK Stiefel              | Physiogel <sup>®</sup> hypoallerg... | 859R                 | 1       |

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| Supplier           | Substance                            | Batch             | Spectra |
|--------------------|--------------------------------------|-------------------|---------|
| GSK/Stiefel        | Physiogel <sup>®</sup> hypoallerg... | 538T              | 1       |
| PHOENIX 21.10.2013 | Physiogel <sup>®</sup> hypoallerg... | 1142N             | 1       |
| Phoenix/Stiefel    | Physiogel <sup>®</sup> hypoallerg... | 399P              | 1       |
| Stiefel            | Physiogel <sup>®</sup> hypoallerg... | 926Q              | 1       |
| Stiefel            | Physiogel <sup>®</sup> hypoallerg... | 270T              | 1       |
| Stiefel            | Physiogel <sup>®</sup> hypoallerg... | 537T              | 1       |
| Stiefel/Noweda     | Physiogel <sup>®</sup> hypoallerg... | 163R              | 1       |
| Stiefel/Sanacorp   | Physiogel <sup>®</sup> hypoallerg... | 10000             | 1       |
| Dyckerhoff         | Regeneresen                          | 60611dü-2         | 1       |
| Dyckerhoff         | Regeneresen                          | 150173th-2        | 1       |
| Dyckerhoff         | Regeneresen                          | 1202920v-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 <sup>TM</sup>              | 1503256           | 1       |
| Fagron             | Versatile <sup>TM</sup>              | 14B19-T02-010391  | 2       |
| Fagron             | Versatile <sup>TM</sup> Rich         | 247224-0002       | 1       |
| Fagron             | Versatile <sup>TM</sup> Rich         | 14B19-T04-0130395 | 1       |
| Fagron             | Versatile <sup>TM</sup> Rich         | 1503257           | 4       |
| Phönix             | Versatile <sup>TM</sup> 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).

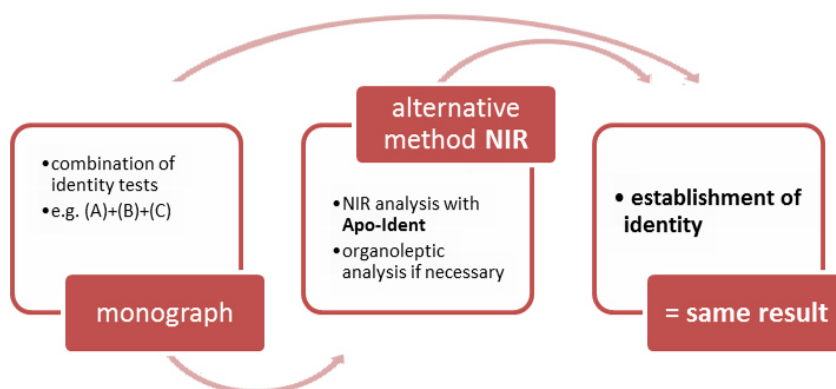


**Figure 2:** The combination of tests of the monograph is replaced by the alternative method NIR spectroscopy using *Apo-Ident*. This is permissible because both test procedures result in the establishment of the identity of the raw material.

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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